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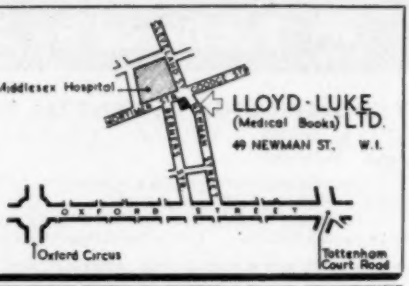

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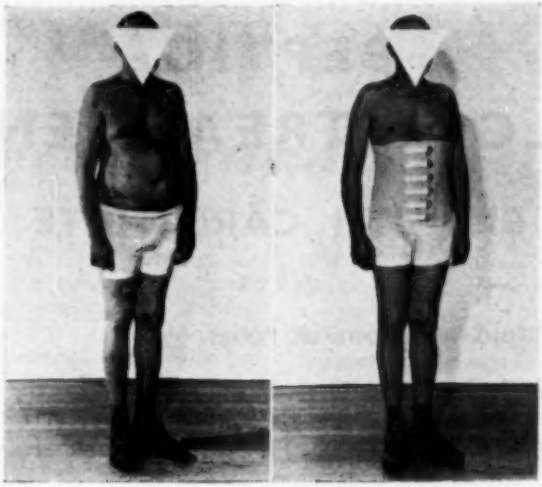

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[1]Lancet, B.M.J. (May 10th and 17th) 1952.
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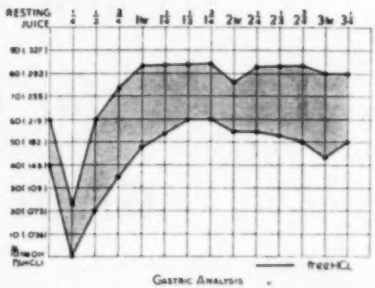

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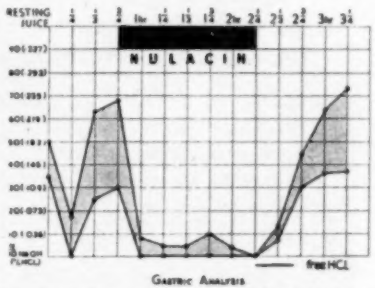

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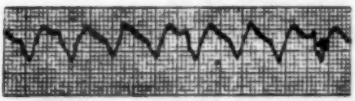

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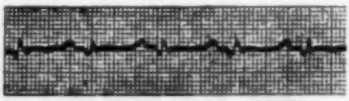

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Successful Clinical Practice spreading over many years is proof of the trustworthiness of THE ORIGINAL PRODUCT. Standard works on cardiology and current medical literature contain numerous references to the unfailing reliability and constant activity of NATIVELLE'S DIGITALINE. Literature, charts and samples will gladly be forwarded on request.

Supplied in the following forms: TABLETS (Pink) 0.1 mg. (1/600 gr.). TABLETS (White) 0.25 mg. (1/240 gr.). AMPOULES for intramuscular and intravenous injection 0.2 mg. (1/300 gr.).

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VAGINAL GEL

the simple method of contraception that needs no diaphragm . . .

Physicians and patients have long been demanding a simpler contraceptive method than jelly and diaphragm.

the barrier is in the base

To replace the function of the diaphragm, a new and better physical barrier, incorporated into the Gel itself, was needed—one that could be depended on to cover the cervical os effectively. The new base of PRECEPTIN, achieved by blending recently developed synthetic gel-forming agents, meets this requirement, making it possible to do away with the diaphragm.

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Of 3760 patients using Preceptin Gel - 99.2 per cent received complete protection

Preceptin's new base :

1. **adheres well to the moist cervical mucosa—forms a persistent, adherent physico-chemical barrier over the cervical os.**
2. **is more miscible with semen—means greater spermicidal potency.**
3. **rapidly releases active spermicides—enables Preceptin to kill sperm on contact.**

Preceptin Vaginal Gel

Used with measured-dose applicator.

COMPOSITION : PRECEPTIN contains the active spermicidal agents p-diisobutylphenoxypolyethoxyethanol 1·00% and ricinoleic acid 1·17% in a synthetic base buffered at pH 4·5.

Preceptin is a registered trade mark and is protected by world patents.

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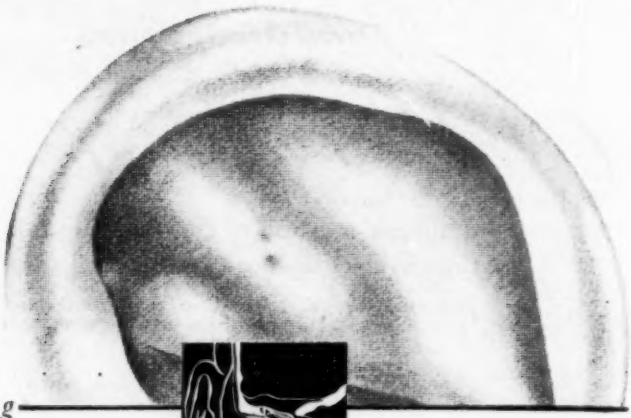

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REFERENCES:
Brit. Med. J., 2:939, 1951
"Treatment of Chronic Otorrhœa and Chloromycetin"
Lancet, 1:541, 1952
"Local Use of Chloromycetin in Wound Infections".

CHLOROMYCETIN TOPICAL
(Chloromycetin 10 per cent in propylene glycol)
is supplied in 5 c.c. vials,
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380

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Following several years of intensive research in the Roche laboratories, 'Rimifon,' isonicotinyl hydrazine, was discovered to be an active antitubercular compound.

The pharmacology of the isonicotinyl hydrazine derivatives has been described (Amer. Rev. Tuberc., 1952, 65, 376), and their activity in experimental tuberculosis ascertained (Bull. Sea View Hosp., 1952, 13, 3).

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Dosage of 'Rimifon' was begun at 2 mg./kg. and later increased to 4 mg./kg., i.e., from one to two tablets three times daily for an average adult.

'RIMIFON' IS ISSUED IN TABLETS OF 50 MG.
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CEDILANID

Attacks of paroxysmal tachycardia respond particularly well to intravenous injections of Cedilanid (Lanatoside C), a crystalline glycoside isolated from *Digitalis lanata*.

In adults, dosage is 0.8—1.6 mg. (4—8 ml.) intravenously. In children, 0.02—0.2 mg. (0.1—1.0 ml.) are recommended, according to age.

The attacks are cut short within 15 minutes to 2 hours. In a series of 16 patients to whom Cedilanid was injected intravenously, normal heart rhythm was restored in 15 patients within an average time of 17.6 minutes (1).

References: (1) Amer. Heart J., 1947, **34**, 871.
(2) Ibid., 1941, **21**, 133.
(3) Ann. int. Med., 1950, **32**, 116.

NOTE: Cedilanid ampoules are supplied ready for use. No dilution is necessary before injection.

Literature and samples available on request

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Pruritus can be particularly difficult in treatment and can be a heavy tax on the physician's time — whether the patient be child or adult. TEEVEX Antipruritic Ointment, however, is a readily available means of allaying the irritation, whatever the origin of the condition. It contains a powerful antihistaminic in combination with crotonyl-N-ethyl-o-toluidide, possesses marked bacteriostatic properties and is presented in a non-greasy, non-staining cream base. In urticarial itching, pruritus vulvae, pruritus ani and summer prurigo, TEEVEX affords prompt and lasting relief.

TEEVEX *Antipruritic Ointment*

In tubes of 20 gms. and 4 oz.

Prescribable on N.H.S. Form E.C.10 · *Literature on request*

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P.H. 42

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FORMULA:

Parachlorophenylether . .	0.5%
Phenylmercuric Nitrate . .	0.004%
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in a Bentonite Cream base

CALPED is also available in powder form where a dry application is desirable.

PACKS: Cream 2 oz. Jars. Powder 4 oz. drums

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Free from side effects **Now available to the Medical Profession**

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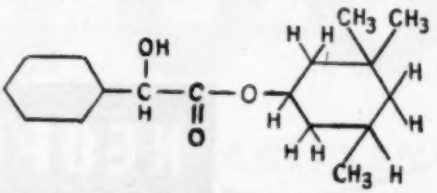

Indications: Ischaemia of the feet, Nocturnal cramps, Diabetic gangrene, Raynaud's Phenomena, Buerger's Disease, Post-phlebitic syndrome, Intermittent claudication and other spastic conditions.

Packings: Bottles of 20, 50 and 250 tablets. Each tablet containing 100 mg. 3 : 5 : 5 trimethylcyclohexylmandelate. Developed and Manufactured by N. V. Koninklijke, Pharmaceutische Fabrieken v/h Brocades Scheeman and Pharmacia, Amsterdam. *May be prescribed on forms E.C.10*

Literature and samples available to the Medical Profession from the sole agents for the U.K.:—

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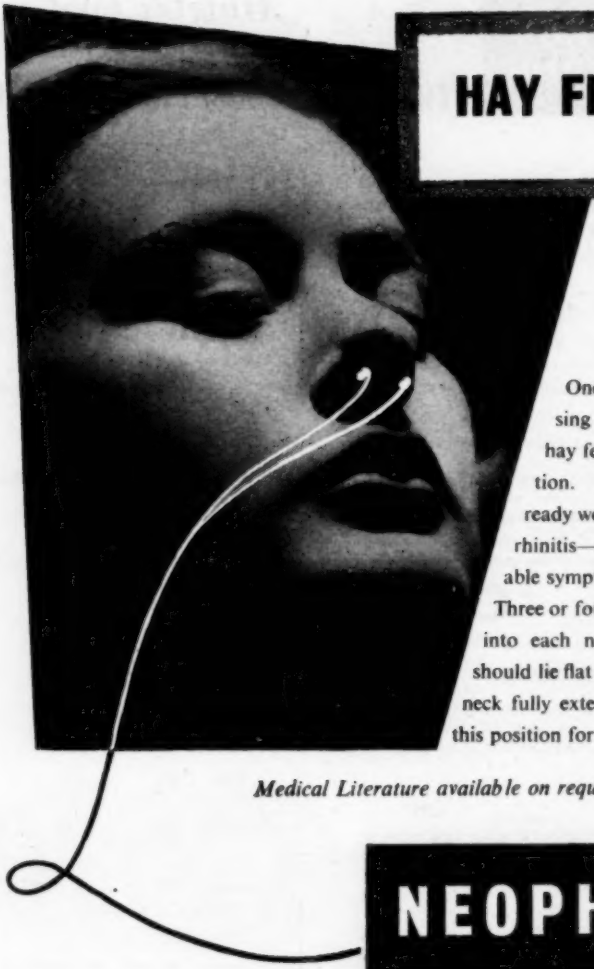

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One of the most distressing accompaniments of hay fever is nasal congestion. NEOPHRYN — already well-tried in colds and rhinitis—may prove a valuable symptomatic aid here. Three or four drops are instilled into each nostril. The patient should lie flat with chin raised and neck fully extended, and maintain this position for two minutes.

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BRAND OF NASAL SOLUTION *Trade Mark*

Neophryn is known overseas as Neosynephrine

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'ESKACILLIN'

the palatable ***liquid*** *oral penicillin*

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50,000 I.U. penicillin per medical teaspoonful (1 fl. dram)

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The new 'Eskacillin' 100 retains all the palatability, stability, freshness, and ease of administration of 'Eskacillin' 50.

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BCP42

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TRIPLE TREATMENT for specific & non-specific DIARRHŒAS

'Cremosuxidine' solves the problem of infant medication — may be given in the regular bottle feeding; any quantity up to 50 per cent of the total volume administered may be added to milk or formula and still pass through an ordinary rubber teat.

1 Checks diarrhœa — helps to produce stools of normal consistency, practically without odour.

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'Sulfasuxidine' Suspension with Pectin and Kaolin

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In the summer . . .

. . . many of those who normally lead sedentary lives go out of doors and indulge in sports and activities to which their musculature is not accustomed. The resulting host of minor athletic injuries — sprains, strains, muscle tenderness, and bruises — may be effectively treated by the application of 'Iodex' cum Methyl Salicyl. rubbed well in till the colour disappears.

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Don't forget to state "C.G. Brand."

Our laboratories operate under Ministry of Health licence (TSA) No. 174. Modern methods and equipment are used and there is constant direct supervision by expert qualified staff. Potency and sterility are absolutely assured. The following are included in our range :—

PENICILLIN ORAL TABLETS— all potencies from 10,000 units to 1,000,000 units per tablet

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INJECTIONS
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Also Pyrogen-free distilled water for the preparation of injections

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LIVER EXTRACT (IM)

A highly potent whole liver extract containing, in addition to the true pernicious anaemia principle, the greater part of the other water soluble active substances in the liver, including particularly the members of the vitamin B complex.

Ampoules — 2 cc. Bottles 10 cc. and 20 cc.

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A concentrated preparation of the uncoagulated juice of liver, fortified with iron and glycerophosphates.

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Capsules containing liver concentrate reinforced with B group vitamins and minerals.

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REGULAR HABITS are undoubtedly the basis of satisfactory bowel movement in the normal individual. Unfortunately, with changes in routine, during illness or convalescence, or due to rush of work and social activities, the habit time of bowel movement is often lost and constipation follows.

Once lost this habit time is not easy to regain, but insistence on a regular effort and the provision of sufficient bulk to stimulate peristalsis will do much to help in its recovery.

'PETROLAGAR' provides soft bulk and achieves a comfortable bowel movement without griping. Gently but surely 'PETROLAGAR' helps the return to habit time.

Issued in two varieties: Plain, and with Phenolphthalein.

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℞ *Veriloid-VP*

VERILOID WITH PHENOBARBITONE

...simplifies the treatment of HYPERTENSION

NOTE

Veriloid, plain, continues to be available in scored tablets of 1 mg. A distinct, biologically assayed fraction of Veratrum viride, Veriloid has given outstanding results in hypertension of all degrees. It produces a significant reduction in arterial pressure without compromise of the postural reflexes necessary for normal living.

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Veriloid-VP is available in bottles of 100 and 500 tablets and may be prescribed on Form E.C.10.

Detailed information sent on request.

Reference: *Lancet*, 261 : 1002 (Dec.) 1951.

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Intensive and prolonged research by British scientists, the pioneers of penicillin, gave this great antibacterial drug to the world. In the field of research and manufacture I.C.I. played a leading and important part and was one of the first manufacturers to produce penicillin in commercial quantities. Since then, I.C.I. have carried out a continuous programme of research and development, and now produce a comprehensive range of penicillin formulations.

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F99 *in the treatment of* ROSACEA

Photograph of Mrs. M. N. taken on July 21st, 1949, before treatment with F "99" Diagnosis: Obstinate Rosacea.

Mrs. M. N.: photograph taken on January 20th, 1950, after treatment with F "99", one capsule daily and daily application of ointment.

F "99" is a concentrate of the active isomer of linoleic and linolenic acids, of standardised biological activity and the highest achievable degree of purity. It is available in capsule, liquid and ointment presentations. F "99" is indicated in cases of Infantile Eczema, Adult Eczema, Rosacea, Furunculosis and other skin disorders associated with a deficiency of essential fatty acids. It is also successful in cases of Varicose Leg Ulcers of long standing.

F "99" has no N.F. equivalent, is not advertised to the public and may be prescribed on EC10. Net cost for example, of treating a typical leg ulcer case is 3s. 6d. weekly.

Literature on request

INTERNATIONAL LABORATORIES LTD. *Dept. PR 11,* **18, OLD TOWN, LONDON, S.W.4**

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75 i.u. per gelucap *Bioglan*

For CARDIOVASCULAR-RENAL DISEASES

Each gelucap contains a concentrate of natural esters (d, alpha tocopheryl acetate) from vegetable oils, type VI, equivalent to 75 mgm. dl, alpha tocopheryl acetate (i.e. 75 international units).

EXTENSIVELY PRESCRIBED ON E.C.10 FORMS IN THE UNITED KINGDOM

VITA-E is the genuine natural Vitamin E used by the Shute Institute and recommended by the Shute Foundation for Medical Research and is sold under no other name. Physicians abroad are warned against using any brand of vitamin E not labelled in terms of international units as per standard of the League of Nations. VITA-E is manufactured in England and is available in all countries so substitutes should be avoided.

Also available a complete range of endocrine and endocrine-vitamin preparations including BIOGLAN-A/R capsules for rheumatism, arthritis, rheumatoid-arthritis and fibrositis (based on the same cortical principle as CORTISONE).

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solution of vitamin B12

'Distivit' B12 is highly effective in the treatment of pernicious anæmia, including the neurological complications of the disease. Megaloblastic bone marrow becomes normoblastic, there is a rapid increase in the red cell count and hæmoglobin level, and clinical symptoms disappear. 'Distivit' B12 is also useful in the treatment of other types of macrocytic anæmia. There are no known contra-indications to its use and there is no evidence that it gives rise to undesirable side-effects. 'Distivit' B12 is issued in three strengths in ampoules containing 20, 50, and 100 micrograms per ml. in boxes of 5 x 1 ml. ampoules.

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THE **Kylon** TRADE MARK

METHOD OF VAGINAL THERAPY
employs
MEDICATED JELLIES
applied by means of
DISPOSABLE APPLICATORS

DEEP PLACEMENT
of medicament without digital insertion and its attendant risk of infection or re-infection.

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of jelly over vaginal surfaces. Note distribution of microscopic acetarsol crystals demonstrating intimate mixture of vaginal contents and the medicament (Kylon Acetarsol Combination).

PROLONGED RETENTION
It is to be noted that, 72 hours after first medication, acetarsol crystals can still be seen.

PACKS Single Sets containing 1 tube of medicated jelly and 12 KYLON applicators *(patent pending)*. Also in HOSPITAL PACKS.

THE FOLLOWING MEDICAMENTS ARE AVAILABLE:—
Acetarsol · Lactic Acid · Sulphathiazole
Oestrone · Proflavine · Ichthammol
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(active against Trichomonas and associated infections).

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the target is the seat of infection within the bowel wall

'ENTEROCID' (Phthalylsulphacetamide) is a powerful bacteriostatic agent for use against intestinal pathogens. It is one of the least toxic of all sulphonamides in contemporary use and attains a high concentration in the tissues of the intestinal wall without being absorbed into the systemic circulation to any appreciable extent.

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(PHTHALYLSUPHACETAMIDE)

Available as:—Tablets containing 0.5 Gm. Containers of 25, 100 and 500.

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SEDATIVE • ANTISPASMODIC • CARDIO-TONIC

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Ext. Crataegus Ocyacanth. Liq. *Sweetened aqueous vehicle*

Exercising a calming and regulating effect on the nervous system, with antispasmodic action, Passiorine forms an invaluable medication for vagosympathetic disturbances. Free from toxicity and habit formation it is ideal for prolonged courses of treatment and is particularly suitable during the MENOPAUSE and in functional disorders of the heart.

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PACKING bottles of 100 c.c.
Dispensing Packs: Bottles of 16 and 80 fluid ounces.

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Literature on application

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ANALGESIC · RESOLVENT · COUNTER-IRRITANT

A solid embrocation without disagreeable :: odour. Will not stain clothing ::

Indications	Action
RHEUMATIC & MUSCULAR PAINS NEURALGIA & HEADACHES BRONCHITIS, CATARRH LARYNGITIS	*The analgesic properties in Ralgex afford rapid relief of all rheumatic and other pains. Ralgex acts as a counter-irritant in cases of Bronchitis, Catarrh, Laryngitis or Pharyngitis.*

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SUCCINATE-SALICYLATE THERAPY

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IN TABLET FORM

For the relief of symptoms
and aid in the control of the systemic metabolic
disturbances found to be associated
with Arthritis and all Rheumatic
disorders

INDICATIONS

1. Rheumatic Fever.
2. Articular Rheumatism (including Rheumatoid and Osteo-Arthritis).
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4. Arthritis associated with the menopause.
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FUNCTION

A stimulating effect on cellular respiration and respiratory enzyme systems, together with an increase of oxygen utilisation by the tissues (impairment in tissue oxygenation having been demonstrated in arthritis).

Since Berex is non-toxic it may be prescribed whenever massive salicylate therapy is indicated.

BEREX combines the following advantages: Prompt relief of symptoms; correction of impaired tissue oxidation; obviation of salicylate toxicity; suitability for protracted administration.

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Despite half a century of painstaking research, there is still no unanimity of opinion regarding the causation of rheumatic diseases. Treatment is therefore necessarily symptomatic and directed to the relief of pain.

Massage has long been the treatment of choice. But in severe cases adequate massage cannot as a rule be begun at once; the affected muscles are too taut and tender. Days or even weeks may have to elapse before the patient can benefit from the stimulating effects of deep massage.

This 'time-lag' has now been eliminated by the use of Lloyd's Adrenaline Cream.

Gentle massage over the affected myalgic spots with this cream brings rapid relief from pain and permits of more intensive treatment than would otherwise be possible.

Supplies of Lloyd's Adrenaline Cream are now available through Boots, Timothy Whites & Taylors, and all pharmacists.

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'ALUDROX' is available as an amphoteric gel in 6 oz. and 12 oz. bottles and as tablets in boxes of 60.

Fundamentals

The action of pepsin in a highly acid medium retards healing of peptic ulcer and predisposes to its recurrence. The fundamental of treatment is, therefore, reduction of acid to a non-corrosive level at which healing can proceed.

'ALUDROX' buffers gastric acid to the safe level of pH 3.5—4.0 at which the ulcer is protected and normal digestion of a bland diet is unimpaired.

'Aludrox'

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Aluminium hydroxide gel

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Successor to salicylate treatment in Rheumatic Diseases—

SODIUM GENTISATE

GABAIL

The sodium salt of 2:5 dihydroxybenzoic acid

Sodium Gentisate (Gabail) gives results similar to large doses of salicylate with, however,

No tinnitus or aural symptoms.

No significant increase in prothrombin time.

No gastric irritation.

No lowering of alkaline reserve. (Simultaneous administration of bicarbonate is therefore unnecessary)

Dosage:
Upwards of two tablets t.i.d.

Presented as brown sugar-coated tablets in bottles of 60 and 500

An increasing number of clinical reports and testimonials confirm the value of Sodium Gentisate (Gabail) in

ACUTE RHEUMATIC FEVER
RHEUMATOID ARTHRITIS
ARTICULAR RHEUMATISMS

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muscular pain

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TRAUMA and inflammatory conditions lead to a muscular spasm with associated pain and stiffness of the affected part. These symptoms are often out of all proportion to the useful results achieved by the immobility of that part, and can be reduced with benefit to the patient. Massage with the anti-spasmodic cream Drenalgin Co. brings about this relief.

Drenalgin Co. (LLOYD)

- Contains adrenaline, ephedrine and camphor in a special base which quickly penetrates the skin.
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- Leads to quick and permanent improvement in the majority of "Rheumatic" conditions.
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No single drug is effective—even the antibiotics

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DECONGEST
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and is active against a wide range of organisms.

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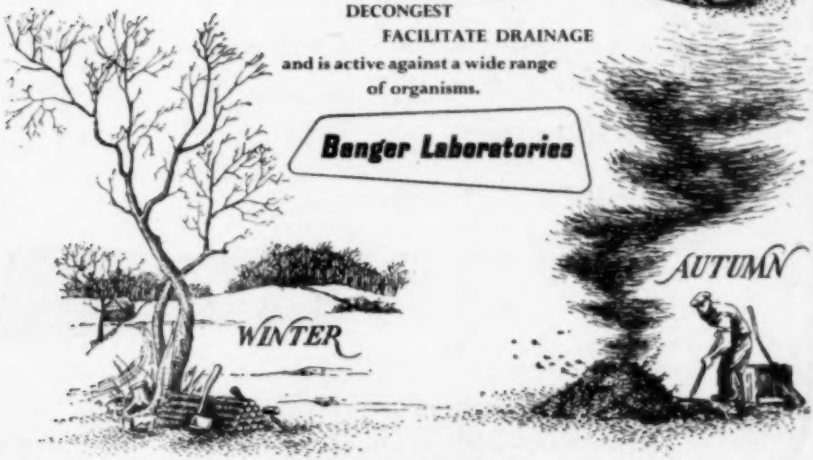

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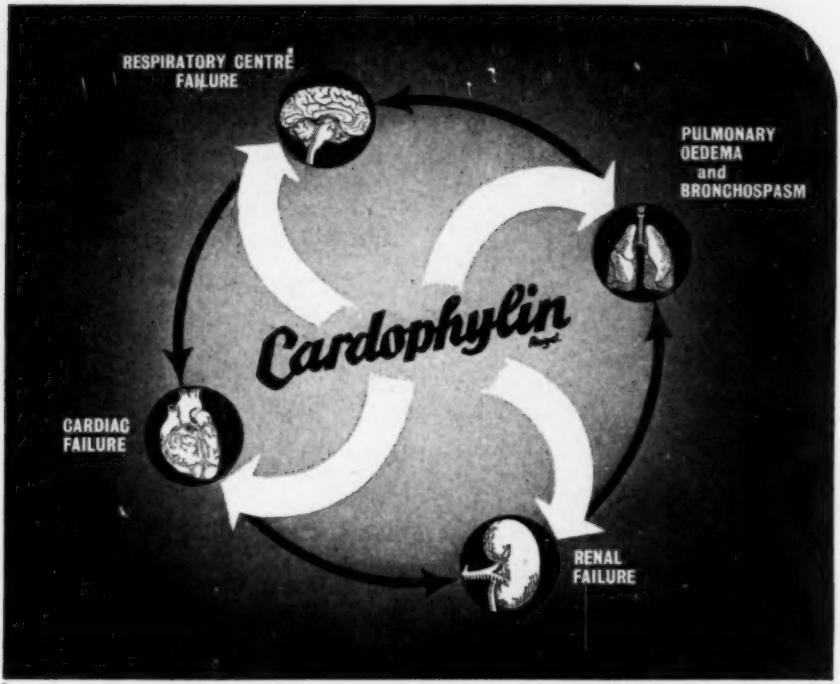

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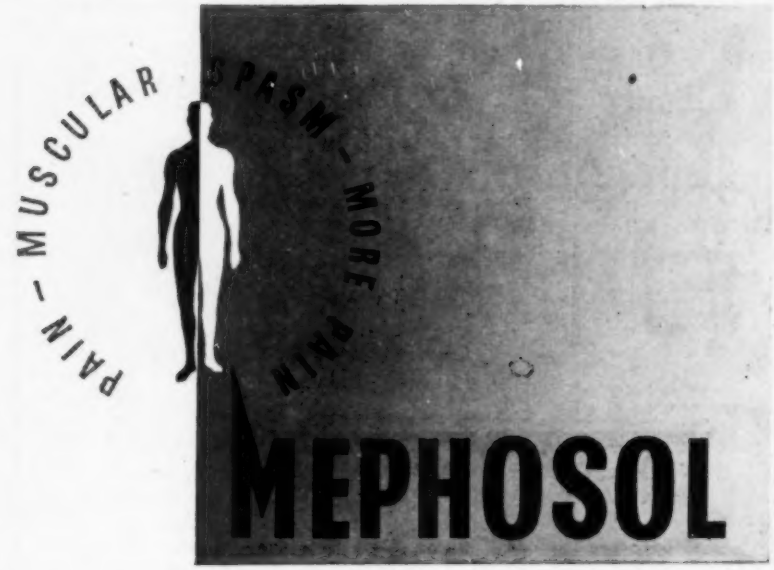

In rheumatic disorders the commonest symptom, and the most trying to the patient, is pain. Following the pain comes muscle spasm, which leads to disability, loss of function — then more pain, more spasm. MEPHOSOL (containing mephenesin) breaks this vicious circle by the direct abolition of skeletal muscle pain. It is analgesic and antispasmodic.

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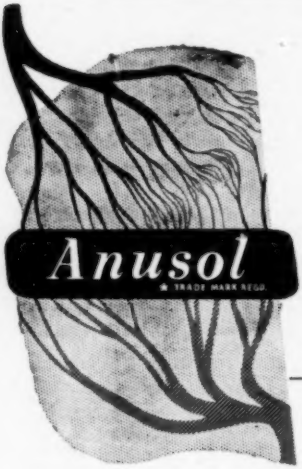

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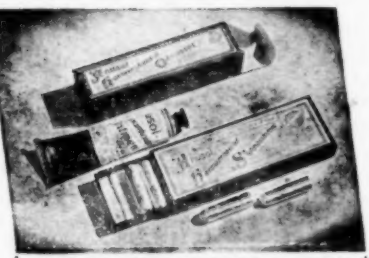

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'Neuro Phosphates' ('Eskay')

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Combined Oral Penicillin and Sulphonamide Therapy

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Alimex acts without liberating carbon dioxide, so that there is no risk of acid rebound.

After the administration of Alimex the stomach contents remain sufficiently acid to permit normal digestion to proceed without interruption.

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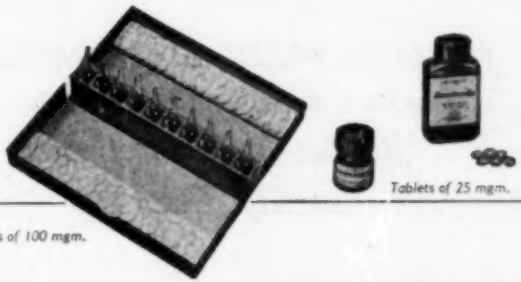

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Tablets of 25 mgm.

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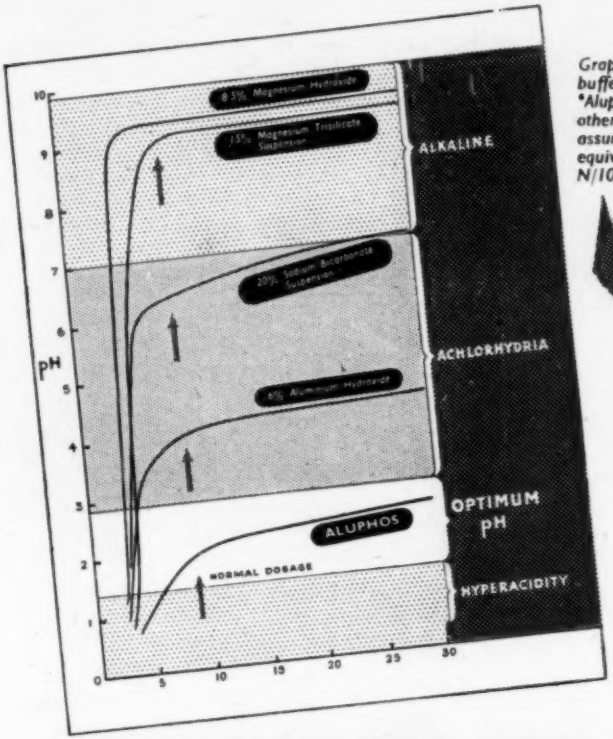

Graph showing the buffering action of 'Aluphos' compared with other common antacids assuming that the equivalent of 100 mls. N/10 acid are present.

In the PEPTIC ULCER PATIENT where hyperacidity must be controlled, Aluphos provides effective pain relief but cannot produce acid rebound

Aluphos BRAND **(ALUMINIUM PHOSPHATE GEL)**
the new, non-constipating antacid

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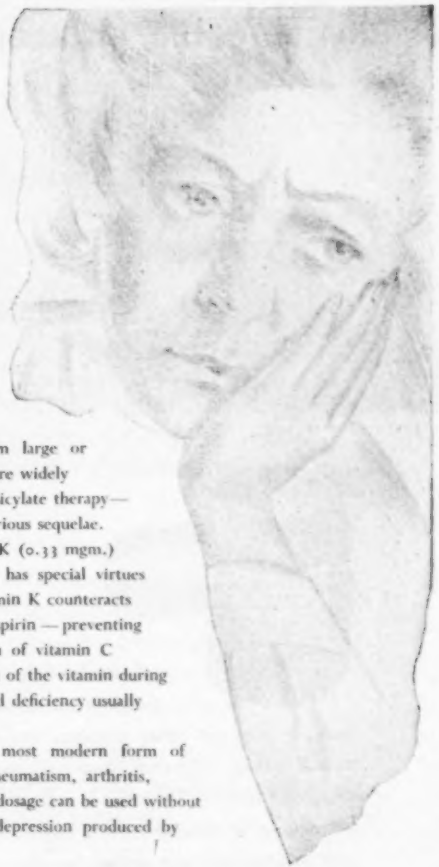
Safer salicylate therapy



The possibility of toxic reactions from large or continuous doses of salicylates is now more widely recognised. The modern approach to salicylate therapy—using EKAMMON—overcomes these serious sequelae. Containing aspirin (0.33 gm.), vitamin K (0.33 mgm.) and vitamin C (25 mgm.), EKAMMON has special virtues as an analgesic and anti-rheumatic. Vitamin K counteracts the prothrombin-reducing action of aspirin—preventing hæmorrhagic tendencies. The addition of vitamin C compensates both the increased excretion of the vitamin during salicylate medication and the ascorbic acid deficiency usually associated with rheumatic patients.

EKAMMON is now regarded as the most modern form of salicylate therapy, of unique value in rheumatism, arthritis, fibrositis and dysmenorrhœa. Intensive dosage can be used without the risk of systemic reactions and the depression produced by salicylates alone.

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whether of varicose, decubital, ischaemic, or diabetic origin, often respond rapidly to the local application of 'Furacin' Soluble Dressing.

'Furacin' Soluble Dressing is active against a wide range of both gram-negative and gram-positive organisms; it does not delay healing; and it produces a marked reduction in wound odour. Bacterial drug-resistance to it has not yet been reported. 'Furacin' Soluble Dressing is indicated for the prophylaxis and treatment of infection in wounds, severe burns, cutaneous ulcers, and skin-graft sites, and for abscesses and carbuncles *after incision.*

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(0·2% nitrofurazone in a water-miscible vehicle)

AN ADVANCE IN ANTIBACTERIAL THERAPY

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In the management of gastro-intestinal disorders associated with hyperchlorhydria, "' Milk of Magnesia' Tablets have proved of outstanding value.

Exerting an immediate and prolonged neutralising action, ' Milk of Magnesia ' Tablets offer a valuable prescription to the physician for the treatment of simple digestive upsets, including gastritis and duodenitis, and equally so, for those cases where frank ulceration has occurred.

Pleasantly mint flavoured and conveniently portable, they are always ready to hand whenever the need of alkalisation arises.

'Milk of Magnesia' TABLETS

Available in bottles of 30, 75 and 150 tablets.

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"' *Milk of Magnesia' is the trade mark of Phillips' preparation of magnesia.*

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Effective, Convenient....

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Cream

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ALOCOL, the reputable brand of Colloidal Aluminium Hydroxide, is now obtainable as a stable, palatable cream, thus presenting with Alocol Powder and Alocol Tablets three methods of administration to meet every condition and preference.

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ALOCOL Cream is supplied in bottles of 9 fl. oz.

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'Alocol,' in all its forms, is a strictly ethical product; it is not advertised to the public.

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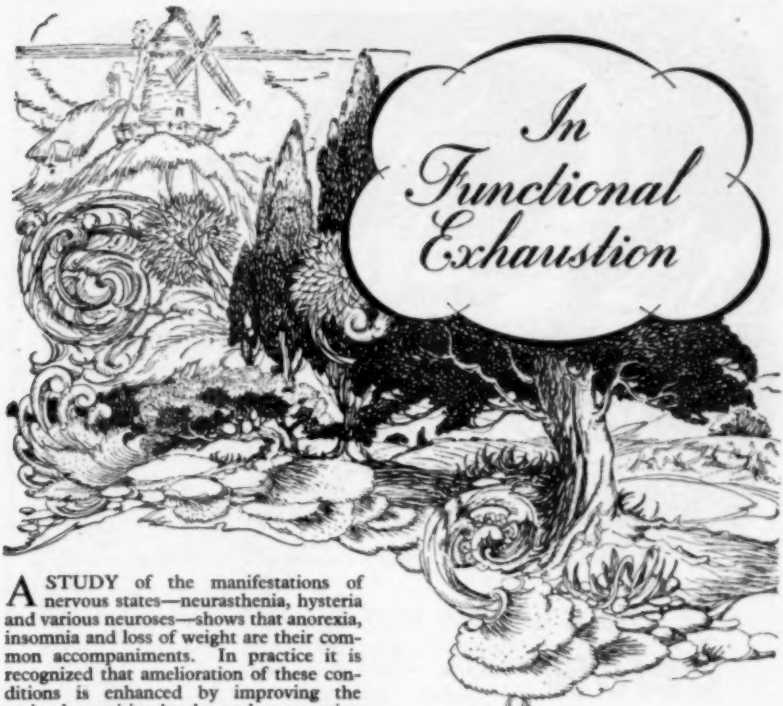

In Functional Exhaustion

A STUDY of the manifestations of nervous states—neurasthenia, hysteria and various neuroses—shows that anorexia, insomnia and loss of weight are their common accompaniments. In practice it is recognized that amelioration of these conditions is enhanced by improving the patient's nutrition by day and encouraging tranquil sleep by night.

'Ovaltine', which contains essential food principles, provides sustaining food elements in acceptable, readily assimilable form which allows digestion to proceed without interrupted sleep. This important consideration is particularly valuable in the treatment of nervous dysfunctions, including exhaustion and anorexia.

'Ovaltine'—the natural food drink—is a confident choice wherever physical upbuild and recuperative sleep are indicated in nervous disorders.

Vitamin Standardization
per oz.—Vitamin B_{12}, 0.3 mg.;
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COMPOUND UNDECYLENATE OINTMENT
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INTRODUCING

PENICILLIN INHALATION SET

FOR NASAL AND ORAL INHALATION

EACH SET CONTAINS—
One inhalator and two vials each containing three capsules 100,000 units crystalline penicillin potassium salt

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For fairly prolonged hypnosis and day-time sedation

TRADE MARK **'AMYTAL'** BRAND AMYLOBARBITONE in strengths of gr. $\frac{1}{8}$, gr. $\frac{1}{4}$, gr. $\frac{1}{2}$, gr. $\frac{3}{4}$, gr. $1\frac{1}{2}$

For medium onset and duration, and especially in the neuroses

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To combine rapid onset with a more prolonged action

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THE PRACTITIONER

No. 1009 JULY 1952 Volume 168

THE MONTH

'CARDIOVASCULAR diseases', the subject of our symposium this month, can literally be described as the most fundamental branch of medicine. So long as the heart beats there is life no matter how damaged the other organs of the body may be. Three of the major advances in cardiology are dealt with in this symposium. In the first place there is the increasing emphasis upon the importance of 'the clinical assessment of cardiac efficiency', and we are particularly fortunate to have obtained the services of Dr. Paul White of Boston, the international doyen of clinical cardiology, to review this important problem. The second major advance is the dramatic entry of the surgeon into cardiology; a development which is ably and practically discussed by Mr. Holmes Sellors. Thirdly, there are the advances in methods of diagnosis, without which much of modern cardiac surgery would be of little avail. Of these new methods, cardiac catheterization is one of the most important, and the practical aspects of this subject are summarized by Dr. J. F. Goodwin. There has been a tendency of recent years for inexperienced workers to use cardiac catheterization indiscriminately. As Dr. Goodwin points out, the method is not without danger, but in the hands of the expert, cardiac catheterization provides vital information which could not be obtained otherwise. 'Cardiac disease in pregnancy' is a subject of which the Manchester School of Cardiology has made a particular study, and Dr. Morgan Jones, a prominent member of this school, demonstrates well the marked improvement which has developed in this important field. The arrhythmias always occupy an important place in cardiological practice, and Dr. Alastair Hunter's article reviews the present accepted lines of treatment, including the relatively new drug in this field—procaine amide. Finally, but by no means least important, is that ever-recurring fear of the layman—'sudden death due to heart disease'. Dr. Oram's article is a practical review of this important problem in general practice.

The Symposium

WE are a conservative profession—and rightly so. When health and life are at stake we are not justified in lightly giving up the accumulated wisdom of the past in favour of what is new but often unproven. On occasions, however, we allow our innate conservatism to obstruct the introduction of measures which can bring nothing but benefit. A case in point is the replacement of the imperial system of weights and measures by the metric system. This is a change which has been under active consideration for many years. A quarter of a

The Metric System

century ago the more progressive pharmacologists were teaching the metric system of prescribing to their students. Clinicians, however, were slow to give up their drachms and scruples, and even the adoption of the system by the *British Pharmacopœia* made little impression. Our pharmaceutical colleagues have always been more progressive in this respect, and their latest move in pressing forward this reform is the adoption by the Association of British Pharmaceutical Industry of a resolution that 'solids, liquid galenicals and pharmaceutical chemicals should be sold in metric weights and measures'. The time has surely come now when the medical profession should take active steps to come into line with our pharmaceutical and scientific colleagues and with our medical colleagues abroad.

Committees Unlimited

In 1950 the Central Health Services Council appointed a committee 'to consider and make a report on—(a) Existing forms of cooperation between (i) Regional Hospital Boards, Hospital Management Committees, Boards of Governors; (ii) and local authorities; and (iii) Executive Councils. (b) Whether it is possible to formulate any general principles on which cooperation might be promoted between these authorities'. In its report, which has now been published ('Report on Cooperation between Hospital, Local Authority and General Practitioner Services'. London: H.M. Stationery Office, 1952, price *1s. 6d.*), the committee state that they 'have come by a process of elimination to the conclusion that a solution must be sought by the creation of general standing joint liaison advisory committees between the various authorities concerned'. In a supplementary memorandum, the Hon. Arthur Howard, a member of the committee, states: 'The main recommendation of the draft report is the creation of an indefinite number of additional committees. While I do not dispute the possibility that some good results might be achieved in some instances, I have come to the conclusion that such a mass creation of additional committees would, on balance, do more harm than good'. As an alternative he advocates greater confidence in the initiative of the members of the Service, both voluntary and paid, an increased degree of decentralization, and a greater flexibility in the administration of the Service.

This minority report is a refreshing gleam of common sense in the fog of bureaucracy which is steadily permeating the National Health Service. On the other hand, it is disturbing to find that the Central Health Services Council is apparently so in tune with the methods of Whitehall that, in spite of evidence of reluctance, it feels impelled to put forward a scheme, the only justification of which is that it fits into an office-born method of administration. If this is the effect of contact with Whitehall upon able and respected leaders of the profession, then the outlook for the future of medicine is indeed bleak. We cannot help feeling, however, that Mr.

Howard's is the opinion that will command the respect and approval of all who place professional standards of conduct before everything else. Whether protests such as his will have any effect in preventing the further multiplication of committees, that noxious invention of bureaucracy, time alone will tell. For the sake of our patients we trust that it will.

Phantom Limbs

SOME image of the missing limb is usually present after amputation, but its reality is very variable. The foot and the hand are always there, the knee and the elbow usually, but the intermediate parts are absent or recognized in but a shadowy form. The phantom usually becomes less real as healing proceeds, and disappears about the time that the skin incision has become avascular and the stump is ready for a prosthesis.

The persistence of a painful phantom is a real disability, one very difficult to dispel. Percussion of neuromas, nerve resection pursued right up to the plexus, even anterolateral cord section may fail to give relief, for if the body wishes to convey a sensation of pain to the brain it will usually succeed. In a recent discussion on phantom limbs at the Mayo Clinic (*Proc. Mayo Clin.*, 1952, **27**, 110) the important part played by psychological factors was stressed. Dr. Adelaide Johnson pointed out that the contemplated loss of a hand or leg arouses in every man a feeling of sadness for the long familiar part that is to go for ever. He secretly studies the condemned member, trying to fix in his memory every scar and wrinkle, and he wonders almost with panic, about its disposal; will it be dumped in a can with all kinds of rubbish, or will it be handled with respect? A frank discussion before operation, indicating that he understands the patient's anxiety and inquiring kindly as to his views about the disposal of the lost member, will enable the surgeon in most cases to avert the development of a phantom limb.

Television —Blessing or Blight?

THE æsthetic and social hazards of television do not concern us here. The potential medical hazards, however, are of the utmost importance to us all as doctors. In his annual report for 1950-51, Dr. J. L. Dunlop, the School Medical Officer for Hertfordshire, has some comments to make on the subject which suggest that these hazards are by no means non-existent. 'Shortage of sleep is still apparent amongst the school population. The children look permanently tired and drowsy in class. After questioning a number of these children it seems that television has aggravated the difficulty of getting them early to bed. When there is a set in the house there is a programme to watch every night instead of them staying up only two or three nights a week to visit the cinema. . . . The white drawn faces and tired eyes still do not persuade parents to use their authority. . . . Perhaps

before long "Television Syndrome" or "Cathode Rayitis" will make an unfamiliar appearance in up-to-date medical textbooks. If common sense and discipline do not again prevail when the novelty of the new medium has worn thin it seems that the new technique, whatever its educational or social implications, will not be an unmixed blessing to the younger generation. Apart from the harm done by constant late hours, there is also the effect of eyestrain to be considered upon those with defective vision.'

It might be argued that similar criticisms could be levelled at the cinema, but this does not invalidate the implications of Dr. Dunlop's observations. Whilst the primary responsibility must be laid upon the parents of the country, it is equally clear that it is the duty of practitioners to advise parents of the ill-effects which television addiction may have upon their offspring.

It's a Boy

More old wives' tales have probably been woven around the means of foretelling the sex of the unborn child than any other aspect of human life. It now looks, however, as if even this mystery of life had been torn asunder by the all-pervading scientists. At least, two American scientists claim to have achieved an impressively high standard of accuracy in 'prenatal sex determination' (Rapp, G. W., and Richardson, G. C., *Science*, March 7, 1952, **115**, 265). Their test was discovered quite accidentally as the result of investigations carried out in elaboration of the Richardson pregnancy test (Richardson, G. C., *Amer. J. Obstet. Gynec.*, 1952, **61**, 1317). This test is based on a urinary reaction, and it was while investigating the reaction of other body fluids, such as saliva, that the possibility of sex prognostication was discovered. In women at the sixth or seventh month of pregnancy it was noted that although the test was always positive in the urine, it was positive in the saliva in only a number of cases. 'The apparent answer to the problem was forthcoming only after the delivery of the child. In nearly every case, the positive tests were associated with a male child, and most of the negative tests were associated with a female child.' The final figures showed that in 221 male births the test was positive in 218, whilst in 155 female births only seven were positive. The precise nature of the substance responsible for the positive test is not known, but the authors believe that 'some androgenic substance is being identified'. In support of this hypothesis they report that 'whereas a nongravid female normally yields a negative test, after the injection of testosterone or androsterone a strongly positive reaction results'. Whatever the explanation, the correlation shown is most impressive and, as the test is a relatively simple one, it should not be difficult for other observers to repeat the work.

THE CLINICAL ASSESSMENT OF CARDIAC EFFICIENCY

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ONE of the most useful medical, social, and economic advances of our day would be the introduction of the clinical assessment, completely accurate or near it, of cardiac efficiency or, for that matter, of the efficiency of any organ in the body, not only for the moment, but for the months and years to come. This ideal is doubtless beyond our reach, but it is worth while to review present possibilities and the ways in which we may progress.

There are several reasons why the assessment of present and future cardiac efficiency is so important today. The most significant reason is the vast increase in the prevalence of heart disease and of crippling and death therefrom during the past generation. This applies particularly to the middle-aged man who is responsible for leadership in business and professional and public life, or in the physical tasks of daily living. A second compelling reason is the need for trying to forecast the future heart health of individuals before disease becomes evident. And a third important reason is to try to estimate the hazard of physical and mental stress on hearts already damaged, especially now, when life, which should continue to be useful and happy, can be prolonged almost indefinitely by the control of infections, and at a time when the employment of cardiac patients is being fostered.

A difficulty of the past has often been the attempt to devise one special test that will do everything in assessing cardiac efficiency without the realization of the need of viewing the person and his problems as a whole. It is, of course, obvious that there is a great range of efficiency required according to the job or tasks to be faced. Thus a stevedore must be more fit physically, in general as well as in his heart, than the man who checks off the things the stevedore carries. Also the liking and aptitude for a job are often as important as the strain therefrom; a man or woman who is accustomed to a task or who is interested therein may be better able to do it than to do something else which seems easier physically but which requires special effort for adaptation or which is repugnant.

Finally, of the greatest importance in these introductory remarks, is the necessary insistence on prophesy as to the future in any given case. A man may be extremely fit for the moment and pass all special efficiency tests with flying colours, but if he has clear evidence of valvular heart disease, for example, slight to moderate aortic stenosis, or of elevated blood pressure (not to be ascribed to a simple hyper-reaction), or of gross obesity, or of diabetes, or of hypercholesteræmia, such a finding must be taken into consideration and some plans laid for adequate check-ups in the future, and

modification, even though but slight, of the ways of life with the hope indefinitely to postpone future trouble.

TYPES OF CARDIAC INEFFICIENCY

Leaving aside the person who has a healthy heart but is not capable of undertaking some unusual physical strain to which he is unaccustomed, as, for example, running for a train at the age of seventy after having avoided such effort during the previous twenty or thirty years, there are two main types of cardiac inefficiency or, as commonly called, insufficiency. These are myocardial and coronary. On occasion they are combined. The balance of this article will largely be concerned with their assessment.

MYOCARDIAL INSUFFICIENCY

In the first place it is necessary to ascertain the kind and severity of the particular myocardial strain, for by so doing a reasonably satisfactory prognosis can often be given. The strains that affect the different heart chambers must be distinguished; in particular, of course, those that affect the ventricles.

Left ventricular strains.—There are three common and often serious sources of strain on the left ventricle: hypertension, aortic valve disease (stenosis or regurgitation, or both), and myocardial infarction, acute or chronic. The most threatening of these, even though there is adequate myocardial function at the moment, are malignant hypertension, marked aortic stenosis or regurgitation, especially the latter whether syphilitic or not, and very large infarcts. Such cases will rarely survive more than a few years at best and must be handled with much care to avoid heart failure and sudden death, which are sometimes precipitated by physical over-exertion, emotional crises, serious infections, and overeating, even though these persons may outwardly appear healthy. On the other hand, lesser degrees of all of these conditions are compatible with long lives, good health, and useful occupations. Despite all this, some attempts to avoid excessive strains are wise.

Symptoms and signs of the beginning of serious effects of these strains on the left ventricle should be carefully looked for by reasonably frequent brief check-ups, at least semi-annually, no matter how well special tests of general physical and cardiac fitness are passed at the time of an original examination. Unaccustomed dyspnœa on exertion or at rest, not to be ascribed to acute infection, lung trouble, or neuro-circulatory asthenia, should arouse suspicion of a myocardial responsibility, and occasion study thereof. Physical examination may reveal evidence of an enlarging heart, an abnormality of heart sounds with increased accentuation of the pulmonary second sound or the development of an apical diastolic gallop rhythm, the appearance of a systolic murmur at the apex not previously heard, the finding on sphygmomanometry of the very revealing but widely neglected alternation of the pulse or, in advanced cases, moist, not atelectatic, râles at the lung bases.

Right ventricular strains.—Much less commonly, but often quite as im-

portant, conditions that produce strain primarily on the right ventricle are encountered. The most frequent of these still continues to be mitral valve disease, especially stenosis, but the decrease in the prevalence of rheumatic fever and of rheumatic heart disease now in progress promises during the coming generation to minimize this factor. Other conditions which should be watched because of their production of strain on the right ventricle include, in particular, obstruction in the pulmonary circulation itself as from thrombosis or embolism; chronic diffuse fibrosing pulmonary disease; several types of congenital heart disease, such as atrial septal defects and pulmonary stenosis; and high degrees of kypho-scoliosis. The symptoms and signs that indicate an overtaxing of the right ventricle from these factors, and which should be looked for, are liver pain from early engorgement even before the neck veins are overfull, the development or increase of cyanosis from slowing of the systemic venous circulation, engorgement of the neck veins, which may at first be just barely visible at the upper edge of the clavicles with the thorax at 45 degrees, and beginning dependent œdema.

SPECIAL TESTS FOR MYOCARDIAL INSUFFICIENCY

There are several special tests which may be applied to test the myocardial reserve in doubtful cases, the most convenient of which is that of some simple exercise to which the subject is accustomed, such as walking at varying speeds on the level or upstairs with the observer accompanying him or her and observing closely the development of symptoms or signs of stress such as have already been noted. Or the two-step test popularized by Master (1935) can conveniently be applied, or some other exercise, as on the treadmill with analysis of respiratory gas exchange on special occasions. In the case of industrial employment the actual procedures which the candidate is to carry out can be applied under close observation and repeated as may be necessary to draw final conclusions.

The Schneider test (1920) of physical fitness may also be applied usefully in young adults, but it is, of course, not specific for heart disease. It should be carried out as follows:—

(1) The patient reclines for five minutes. (a) The heart rate is then counted for twenty seconds. When two consecutive twenty-second counts are the same, this is multiplied by 3 and recorded. The score is noted according to part A, table 1. (b) The systolic blood pressure is next taken by auscultation: two or three readings are made as a check.

(2) (a) The patient stands at ease for one or two minutes to allow the pulse to assume a uniform rate. When two consecutive twenty-second counts are the same, this is multiplied by 3 and recorded. The score is obtained by the use of part C, table 1. The difference between the standing and reclining pulse rate is then scored by use of part B, table 1. (b) The standing systolic pressure is next taken. The difference between this and the reclining systolic pressure is then scored by part F, table 1.

(3) The patient next steps on a chair about 18 inches high, five times in fifteen seconds timed by a watch. To make this test uniform, he stands with one foot on the chair at the count one; this foot remains on the chair and is not brought to the floor again until after the count five. At each count he brings the other foot on to the chair

and at the count 'down' replaces it on the floor. This should be timed accurately, so that at the fifteen second mark both feet are on the floor. (a) Immediately, while he stands at ease, the pulse rate is counted for fifteen seconds; this is multiplied by 4 and recorded. (b) Counting is continued in fifteen-second intervals for two minutes, record being made of the counts at 60, 90 and 120 seconds.

The data from (a) will be scored by part D, table 1, taking the difference between this exercise pulse rate and the standing rate. The data in (b) are scored according to part E, table 1.

TABLE 1

POINTS FOR GRADING CARDIOVASCULAR CHANGES IN SCHNEIDER'S TEST OF PHYSICAL FATIGUE AND EFFICIENCY

SCHNEIDER INDEX

A. Reclining pulse rate

Rate	*Points*
50– 60	3
61– 70	3
71– 80	2
81– 90	1
91–100	0
101–110	–1

B. Pulse rate increase on standing (points)

0–10 *Beats*	11–18	19–26	27–34	35–42
3	3	2	1	0
3	2	1	0	–1
3	2	0	–1	–2
2	1	–1	–2	–3
1	0	–2	–3	–3
0	–1	–3	–3	–3

C. Standing pulse rate

Rate	*Points*
60– 70	3
71– 80	3
81– 90	2
91–100	1
101–110	1
111–120	0
121–130	0
131–140	–1

D. Pulse rate increase immediately after exercise

0–10 *Beats*	11–20	21–30	31–40	45–50
3	3	2	1	0
3	2	1	0	0
3	2	1	0	–1
2	1	0	–1	–2
1	0	–1	–2	–3
1	–1	–2	–3	–3
0	–2	–3	–3	–3
0	–3	–3	–3	–3

E. Return of pulse rate to (standing) normal after exercise

Seconds	*Points*
0– 30	3
31– 60	2
61– 90	1
91–120	0
After 120, two to ten beats above normal	–1
After 120, eleven to thirty beats above normal	–2

F. Systolic pressure, standing, compared with reclining

Change in mm. Hg	*Points*
Rise of 8 or more	3
Rise of 2–7	2
No rise	1
Fall of 2–5	0
Fall of 6 or more	–1

The total score is then added up in parts A, B, C, D, E, and F of table 1. The maximum possible is 18 and the minimum is minus 11. A score above plus 9 is considered normal; a score of 9 or less fails to pass and is reason for a search as to the cause.

The *test of the vital capacity*, that is, of the amount of air in millilitres

(ml.) that can be expired after the deepest possible inspiration and measured by spirometer, can be applied usefully if its limitations are recognized. In the first place, some instruction and practice are needed. Secondly, it is much more useful for serial testing than as a single procedure, since the range of normal is wide, for example, $3\frac{1}{2}$ to $5\frac{1}{2}$ litres for adult males and 3 to $4\frac{1}{2}$ for adult females, varying somewhat according to body build and physical training. Also, it should be recognized that pulmonary disease, neuro-circulatory asthenia, and a few other conditions can affect the vital capacity just as readily as congestion of the pulmonary circulation due to heart disease, whether consisting of myocardial weakness from left ventricular strains or of mitral stenosis.

Fluoroscopy and even *x-ray films* may reveal engorgement of the lung hilus shadows or, in extreme cases, pulmonary œdema, especially when carried out immediately after some effort or other strain, confirming the significance of the symptom of dyspnœa.

Determination of the rate of the circulation to the lungs by the injection of ether or paraldehyde into an arm vein (normal range = 3 to 9 seconds) and through the lungs and into the peripheral arteries by the injection of any one of a number of chemicals, e.g. decholin, calcium gluconate, histamine, lobeline, aminophylline, amyl nitrite, sodium cyanide, fluorescein, papaverine, and glucose or saccharin (normal range = 8 to 20 seconds), is useful in rare cases in which there is some doubt as to the cause of dyspnœa or of peripheral œdema or congestion. For special studies these tests are also useful but they are not often needed in dealing with patients in actual practice.

Finally, in testing myocardial efficiency there are still newer methods now being studied, such as *ballistocardiography* and *electrokymography*, but we have not yet sufficient information as to their usefulness for this particular purpose to advise their adoption as routine clinical procedures. Nevertheless, the further investigation of these tests should be followed with interest by the practising physician.

CORONARY SUFFICIENCY AND INSUFFICIENCY

With the increasing prevalence of coronary heart disease and its priority as health problem number one in many countries today, it is of great importance to ascertain who are potential victims of this disease and the earliest possible evidence of its existence. Although little has as yet been accomplished in elucidating the pathogenesis of serious coronary atherosclerosis, we have at least learned to recognize the young candidate. Such is a robust male, preponderantly mesomorphic (muscular and broad) in build, with a tendency to some endomorphy (fat type), and thirty-five to fifty years old, especially if there is a family history of coronary crippling at a relatively early age. The female sex, 'skinny' build (ectomorphy), and considerable familial longevity appear to be distinctly protective. Other conditions which

favour the occurrence of crippling coronary atherosclerosis and which, along with those already mentioned, should cause the practitioner especially to watch and advise the potential cases (e.g., to avoid obesity but not vigorous exercise if there is no evident disease) include diabetes mellitus and hypercholesteræmia.

In suspected cases a past history of coronary insufficiency (angina pectoris) or of myocardial infarction is of the greatest importance in analysing current troubles. Details of past medical observations, including electrocardiograms, should be asked for, but it should be remembered that new and non-cardiac causes of puzzling symptoms may arise, such as cardiospasm (œsophageal pain) with or without a hiatus hernia of the stomach, especially in a person more than fifty years old, to complicate a past history, but not necessarily any present recurrence, of coronary heart disease. And finally, it is common to find, particularly in older patients, several different coincident diseases, including coronary heart disease with angina pectoris. In such cases great care in history taking, rich experience, and sound judgment may be much more important than all the tests in the world. Despite this fact, full utilization of available methods of study may help considerably.

The best test of all for coronary insufficiency is the reaction of the subject to exercise, or excitement as he himself tells the story. Angina pectoris is usually a characteristic symptom, completely isolated, and requiring nothing else in establishing the diagnosis. There are, to be sure, uncommon variations of the location, character, intensity, and radiation of the discomfort, also rare doubtful cases (even a few *sine dolore*), and very rare malingerers, as in the famous New York City Insurance conspiracy of ten to fifteen years ago, and in accident and military hypochondriacs. In such rare cases further special tests may be necessary, but certainly in no more than two or three cases in a hundred.

Angina pectoris.—The symptom of angina pectoris itself is almost always described as a heavy oppression (at times a 'strangling' = angina) under the breast bone on effort or excitement, lasting a few minutes and subsiding more quickly with trinitrin (nitroglycerin) than with rest alone. It may or may not radiate to the arms, more often the left than the right, and it may in rare instances arise peripherally and radiate to the front of the chest. Characteristically it is an isolated symptom in an otherwise healthy middle-aged man who complains of no other symptom such as dyspnœa, palpitation, weakness, or faintness. The more symptoms there are, the less likely is one to be dealing with the angina pectoris of coronary insufficiency, although it is true that angina pectoris may complicate neuro-circulatory asthenia which has been present in a case for many years.

There are no signs characteristic of coronary heart disease on physical examination. There may or may not be any cardiac enlargement; often there is none. There may or may not be any heart murmurs or abnormalities of heart sounds. The blood pressure may or may not be normal. Usually the

rhythm is normal. The fact that there are no characteristic physical signs of coronary insufficiency or coronary heart disease occasioned a considerable delay in recognition of the cardiac responsibility for angina pectoris after it was first presented as a medical problem by Heberden in 1768.

The electrocardiogram.—The one laboratory test that helps most in diagnosing coronary insufficiency is well known to be the electrocardiogram. Although it is true that in a certain considerable percentage of 'coronary patients' (perhaps 25 per cent.) the electrocardiogram may be normal when there is no angina pectoris actually present, it is unusual to fail to uncover diagnostic changes of myocardial anoxia or rather hypoxia, especially elevation or depression of the S-T segments in the præcordial leads over the left ventricle (leads V_4, V_5, and V_6) at the moment of a full-blown attack. Indeed there may be such diagnostic changes in the electrocardiogram on exercise or excitement, or at rest, even though there may be little or no angina pectoris; this is likely to be the case more often in insensitive persons, who are therefore all the more in danger than are nervously sensitive individuals. However, slight inconsequential variations in the normal electrocardiogram due to changes of position or physiological function must not be interpreted as evidence of coronary insufficiency. Already there are today otherwise healthy persons who have been presented with an electrocardiographic neurosis by some inexperienced electrocardiographer. For details of changes in the records that do indicate coronary insufficiency the reader is referred to authoritative modern works on electrocardiography. Suffice it here to say that pronounced elevations or depressions of the S-T segments, inversions of the T waves, and the production of a-v or bundle-branch block are the usual electrocardiographic evidences of coronary insufficiency.

Before leaving the electrocardiogram one may say that the presence of changes indicative of chronic coronary heart disease, as from myocardial infarction in the past, is suggestive of the possibility that current symptoms are due to fresh trouble, but, as already stated, it is common for other diseases and symptoms to be superimposed on chronic heart disease of any type, particularly in later life.

SPECIAL TESTS FOR CORONARY INSUFFICIENCY

Finally, we come to a consideration of special tests for coronary insufficiency. These are rarely necessary and then only in obscure or doubtful cases, or when, for insurance or other purposes, it is desired to secure objective evidence for present or future reference. This statement is, of course, based on the assumption that a very careful history has been taken with whatever additional aid is afforded by the electrocardiogram, consisting preferably of twelve routine leads, 1, 2, 3, aVR, aVL, aVF, V_1, V_2, V_3, V_4, V_5, and V_6.

The simplest special test is, of course, that of *exercise*, and one of the most simple exercise tests is that of a walk on the level at varying speed with an observer watching the patient, testing the effect of trinitrin (nitroglycerin),

consisting of a 1/200 or 1/100 grain (0.32 or 0.65 mg.) quickly soluble tablet under the tongue, and, if necessary or desired in addition, taking an electrocardiogram (especially, and beginning with, the præcordial leads over the left ventricle). Or *Master's two-step test* (1935, 1950) can be used for the exercise: this consists of going back and forth over a frame of two steps, each 9 inches high, at a rate of from 15 to 30 round trips, varying according to weight and age, in 1½ minutes. Or a circular staircase frame may be used, such as that described by Nylin. In any event the point at which angina pectoris is first felt is recorded and an electrocardiogram is taken. Because of the possible hazard, however, even though remote, from any one attack of angina pectoris, it is in my opinion wisest to reserve all special tests for the truly rare doubtful cases or for special important researches.

Another test of coronary insufficiency is that of the *inhalation of low oxygen air* introduced by Levy (1938). Ten per cent. oxygen and 90 per cent. nitrogen are inhaled by the subject to the point of the onset of angina pectoris or for a total duration of twenty minutes, at which time 100 per cent. oxygen is given. An electrocardiogram is taken at the height of the effect of the hypoxia. This test has been found useful in some cases but it requires special equipment.

Finally, *ballistocardiography* has been shown to afford abnormal tracings in the presence of coronary heart disease in some cases, but research is still needed to determine whether there is any specific or pathognomonic effect of old myocardial scars, new infarcts, or indeed of current coronary insufficiency. As already stated, it is probably wisest to await final appraisal of the routine clinical usefulness of ballistocardiography until further investigations with follow-up studies have been carried out in adequate numbers of cardiac and non-cardiac patients and of normal controls.

CONCLUSIONS

It seems evident that our present knowledge and experience require a wide appraisal of the clinical assessment of cardiac efficiency, utilizing family and past personal history, symptoms and signs, and various laboratory studies; special tests are rarely necessary, valuable as such tests are in their own right. Current functional capacity alone is not an adequate criterion for sound advice as to the future, especially in these days of the great increase in the prevalence of cardiovascular disease and of the need for utilizing to the full the industrial capacity of our citizens whether or not they have some degree of heart disease. We should, however, continue to improve our present methods of appraisal and to search for still more useful tests of cardiac efficiency.

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THE TREATMENT OF CARDIAC ARRHYTHMIAS

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THE major disorders of the heart's rhythm likely to require correction by treatment are paroxysmal ectopic tachycardia, auricular fibrillation, and auricular flutter. Extrasystoles seldom need treatment, whilst heart block does so only if it is accompanied by heart failure, and is therefore beyond the scope of this article.

PAROXYSMAL ECTOPIC TACHYCARDIAS

These disorders are characterized by sudden bursts of rapid beating arising from an abnormal pacemaker situated either in the auricles or in the auriculo-ventricular node (supraventricular tachycardia), or in the ventricles. The supraventricular tachycardias may be considered together, since their treatment and indeed their clinical features are identical and differ greatly from those of ventricular tachycardia.

SUPRAVENTRICULAR TACHYCARDIA

This is the most common type of paroxysmal tachycardia and occurs generally in people with otherwise healthy hearts. The attacks are self-limited and usually last for less than an hour. Less often they may continue for several days and, exceptionally, for periods of from one to three weeks. The average rate is between 150 to 200 per minute. Ordinarily they are not dangerous and are merely a nuisance, but the longer attacks can cause heart failure, a risk which increases with the length of the attack (Campbell, 1947). The liability to failure is also greater when there is associated heart disease, or when the ventricular rate is very high, e.g., 250 to 300 per minute. Paroxysmal supraventricular tachycardias can occur in infancy, when they are apt to cause early heart failure which may be fatal (Hubbard, 1941; Neubauer, 1945). Paroxysms are believed to be precipitated by a number of causes, including infections both acute and chronic, especially pulmonary infections, poisons such as tobacco and alcohol, gastro-intestinal upsets, excitement, and sometimes hyperthyroidism. Many paroxysms seem to begin spontaneously.

The *treatment* of paroxysmal supraventricular tachycardia includes measures designed to stop the attacks and also to prevent their recurrence. Prevention consists in the elimination of known causes, and the use of drugs, either sedatives such as phenobarbitone over long periods, or quinidine in small doses, e.g. quinidine sulphate, 3 to 5 grains (0.2 to 0.32 g.) thrice daily. Sometimes digitalis folia, 1 grain (65 mg.) twice or thrice daily,

is helpful, but success is uncertain and improvement is often due to a natural remission. Numerous methods have been recommended to deal with a paroxysm, the most reliable being vagal stimulation, either mechanically or by cholinergic drugs, and the use of quinidine and digitalis. More recently, success has been claimed for a derivative of procaine—procaine amide. The majority of attacks stop spontaneously or as a result of some trick known to the patient, and only prolonged attacks or those accompanied by heart failure or occurring in children need treatment. In every case, except in children, vagal stimulation by simple methods should first be tried. Orbital and carotid sinus pressure are the most widely practised, but sometimes self-induced vomiting, or expiration against a closed glottis, is helpful. Orbital pressure must be firm and even painful and should be maintained on both eyes simultaneously for as long as it can be tolerated. The carotid sinus must always be compressed separately on each side. The patient sits or reclines with the neck relaxed while the carotid sinus is compressed or massaged backwards and medially against the spine with the thumb at the bifurcation of the common carotid artery above the cricoid cartilage. Pressure should be maintained for at least 30 seconds and stopped as soon as the tachycardia ceases. Cerebral syncope and hemiplegia are negligible risks with unilateral carotid pressure. Direct vagal stimulation should always be applied early, since it is seldom effective when an attack has lasted long. Cholinergic drugs are more reliable and will generally stop a prolonged attack within a few minutes (Starr, 1936). Mecholyl is the most valuable drug, and can be given in a dose of 10 to 20 mg., injected subcutaneously, and repeated if necessary within an hour. Unpleasant side-effects, such as sweating, salivation, nausea and vomiting, are fairly common, and sometimes there is a sharp fall in the blood pressure. The drug should be used cautiously in the presence of heart failure and also in children, when it can be dramatically successful (Walsh and Sprague, 1940) but may be dangerous. Other cholinergic drugs, such as carbachol and prostigmin, are less efficient.

When a paroxysm has continued in spite of vagal stimulation and mecholyl injections, quinidine or digitalis should be used. Except when there is heart failure, quinidine is preferable and should be given in full dosage, but there is little to choose between the two drugs, and rapid digitalization with intravenous digoxin, starting with 1 mg. and continuing with 0.5 mg. six-hourly, will often stop an attack. In infants, digitalis is the drug of choice, one-sixth to one-quarter of the adult dose being used. It should be given early and continued until it is effective, since an attack in the first year of life is dangerous and may even present with signs of failure.

VENTRICULAR TACHYCARDIA

Ventricular tachycardia is fortunately less common than supraventricular tachycardia. Occasionally benign, it is more usually associated with serious heart disease, particularly hypertensive heart disease and acute infarction.

It is also a recognized complication of anæsthesia, especially with cyclopropane, and of operations on the heart. The prognosis is always serious (Cooke and White, 1943) because of the risk either of failure or of fatal ventricular fibrillation; the need for treatment is urgent. Digitalis is contraindicated, and is indeed sometimes responsible for the onset of the arrhythmias. *Quinidine* is the generally accepted drug and is successful in a high proportion of cases if given in adequate amounts. Except in extreme urgency when failure is established it can be given by mouth: 6 to 9 grains (0.4 to 0.6 g.) quinidine sulphate two-hourly for 5 doses, i.e., up to 45 grains (3 g.) in all, should produce a blood concentration of 4 to 9 mg. per 100 ml., which ought to stop the majority of paroxysms (Sokolow and Edgar, 1950). The course can be repeated on following days and maintained for about a week. Some physicians give larger amounts, up to 90 grains (6 g.) daily, but it is doubtful if they are any more effective in a resistant case. There is a tendency to be over-cautious in the use of quinidine and some prefer to start with 15 grains (1 g.) daily and to increase the dose gradually. There is little to recommend this practice, especially with ventricular tachycardia. The chief disadvantage of quinidine is its toxicity. Signs of cinchonism—tinnitus, headache, nausea, visual disturbances and sometimes vomiting, blindness and collapse—may appear. Quinidine is also a cardiac depressant and can cause serious conduction defects in the heart and a severe fall in blood pressure. The margin between a therapeutic and a toxic dose is small, but risks must be accepted in dealing with paroxysmal ventricular tachycardia and the drug be continued in spite of minor signs. When failure is established, quinidine may be used intravenously: quinidine bihydrochloride, $7\frac{1}{2}$ grains (0.5 g.) in 10 ml. of water, can be given, or 60 grains (4 g.) of quinidine sulphate can be dissolved in 500 ml. of normal saline and given at the rate of 100 ml. hourly (Hepburn and Rykert, 1937).

The discovery that procaine was able to control cardiac irritability (Dawes, 1946) has lead to its use in paroxysmal tachycardia. Unfortunately its value is limited by its depressant effect upon the nervous system and by a very rapid hydrolysis in the body. Esterification of one of its metabolites, diethylaminoethanol with *para*-aminobenzoic acid has produced N′-(2-diethylaminoethyl)*para*-aminobenzamide, or *procaine amide* ('pronestyl'-Squibb). It is too early to assess the place of this substance in treatment, but there is good evidence available to show that it is as potent as procaine without having its undesirable effects on the nervous system. It has been used successfully in single cases, and Mark and his associates (1951) have been able to restore normal rhythm in 13 out of 15 patients with paroxysmal ventricular tachycardia, six of whom had failed to respond to treatment with quinidine. The exact mode of action of procaine amide is not known, but there is reason to believe that it increases the refractory period of the heart muscle and raises its threshold of excitability (Wedd *et al.*, 1951). It can be given orally or by intravenous injection. By mouth it acts after about half

to one hour; intravenously it acts at once, normal rhythm often returning during the injection. Its action continues for about three to six hours but can be renewed by further doses. Procaine amide is liable to cause headache, nausea and vomiting. Its most troublesome effect is hypotension, which is not usually severe but can cause collapse. Toxic symptoms are worse after intravenous injection, and practical experience suggests that they may have been underestimated in earlier accounts. Certainly, intravenous injection should be reserved for emergencies, when a dose of 0.4 to 1.0 g., given at rates of up to 200 mg. per minute, is usually safe and efficient. The injection should be stopped as soon as normal rhythm returns. The oral doses recommended are 1.25 g. initially, followed by 0.75 g. after one hour, with a maintenance dose of 0.5 to 1.0 g. thereafter. In practice these doses sometimes seem to be on the small side and may have to be increased. Procaine amide can be administered to anæsthetized patients and is already proving valuable in suppressing ventricular arrhythmias during operations on the heart. It is too soon to compare the relative merits of procaine amide and quinidine in the treatment of ventricular tachycardia. Procaine amide has undoubtedly been successful when quinidine has failed. It also has the advantage of a relatively rapid action, notably after intravenous injection. Its toxic effects are said to be less severe than those of quinidine, but a limited experience in practice suggests that they may have been underestimated, whilst those of quinidine tend to be exaggerated.

It is generally held that procaine amide is less valuable in cases of auricular arrhythmias, but it is certainly not without effect. It has been used successfully in several cases of auricular tachycardia (McCord and Taguchi, 1951), and also in fibrillation, in which it acts better in the more recent cases (Schaffer *et al.*, 1951). None the less, in these arrhythmias it does not seem to have any advantage over digitalis or quinidine.

Briefly, the treatment of ventricular tachycardia must be regarded as an emergency justifying certain risks. Procaine amide by mouth, except when failure is established, would seem to be the drug of choice, to be followed by quinidine in full dosage if normal rhythm had not been restored after one hour.

AURICULAR FLUTTER

Auricular flutter can be either paroxysmal or established. The diagnosis of paroxysmal flutter is impossible without electrocardiograms, since slow periods of regular beating are a natural feature of the arrhythmia and cannot be distinguished from periods of sinus rhythm. Established flutter is generally associated with structural heart disease, especially mitral stenosis and hypertensive heart disease, although it sometimes appears as an isolated abnormality. Successful treatment is difficult but every attempt must be made to alter the arrhythmia, which is seldom compatible with efficient cardiac function. Full digitalization is undoubtedly the method of choice.

When heart failure is present, intravenous digoxin should be used to obtain a rapid effect, but otherwise digitalis folia can be given by mouth. A dose of 3 grains (0.2 g.) on the first day, 2 grains (0.13 g.) on the second, and 1 grain (65 mg.) on the third, given six-hourly, should produce an effect which should be maintained for at least a week, or until the arrhythmia stops. In a majority of cases digitalis will convert flutter to normal rhythm, either directly or more often after a period of auricular fibrillation. It is usual to stop digitalis when fibrillation begins, but this is not absolutely necessary since continued administration does not preclude a return to normal rhythm.

The choice of digitalis preparations is generally determined by personal preference of the physician and by the urgency of the case. For routine use, tablets of the powdered leaf are reliable, inexpensive and easy to administer. They retain their potency almost indefinitely, although old tablets have a tendency to crumble (Evans, 1940). Tincture of digitalis is seldom used since it is unpleasant, often causing nausea, and liable to deteriorate, whilst the numerous preparations of digitaline vary so greatly that they have little advantage over the whole leaf (Dick, 1948). When rapid effects are necessary digoxin is as effective as any preparation. A single dose of 2.5 mg. by mouth will produce an effect within two hours, and a dose of 2.0 mg. within four hours. Intravenous doses of 1.0 to 1.5 mg. will be even more certain to produce a rapid effect.

Should digitalis fail to restore normal rhythm, quinidine may succeed. Full doses should be prescribed and maintained for a week or until the arrhythmia ceases. Withdrawal of digitalis before starting quinidine is customary but there is no reason to insist on this. Some authorities prefer to maintain it since it will control the ventricular rate, which often rises when quinidine is given (Wood, 1950). If quinidine does not restore sinus rhythm after one week it should be stopped and digitalis continued, with the object of maintaining either fibrillation or flutter with a controlled ventricular rate. Progress should be reviewed from time to time, since a surprising number of cases return to normal rhythm after an interval of weeks or even months. When sinus rhythm has returned, quinidine or digitalis can be stopped. On purely empirical grounds I usually continue small doses of one of them for about two months, to check any tendency to recurrence.

AURICULAR FIBRILLATION

Paroxysmal auricular fibrillation is not uncommon. It is usually a benign disorder comparable with supraventricular tachycardia but with an eventual tendency to become established. Quinidine is the recognized drug for stopping a paroxysm, but digitalis is often effective. It is preferable when there is heart failure, or when there are conditions in which toxic reactions from quinidine are particularly undesirable, as when paroxysmal fibrillation complicates acute infections and postoperative states. A single dose of 1 mg.

of digoxin intravenously, with 0.5 mg. repeated after four to six hours and thereafter as necessary, will generally stop or control the paroxysm. Should fibrillation persist, quinidine can be used in addition. The incidence of recurrent paroxysms of fibrillation can be lessened by maintenance doses of quinidine, 3 grains (0.2 g.) thrice daily, or even of digitalis folia, 1 grain (65 mg.) twice daily.

Established fibrillation.—Auricular fibrillation is generally regarded as established when it has been present for six weeks and is unlikely to cease spontaneously. Established fibrillation is almost always accompanied by gross heart disease, such as mitral stenosis or hypertension, and can be looked upon as an inevitable stage of deterioration in the course of the disease. Failure of some degree is likely to be present, and since the arrhythmia is partly responsible the possibility of conversion to normal rhythm should be seriously considered. When, as is usually the case, there is great enlargement or a history of embolism or severe failure, the question scarcely arises. Control of the failure by digitalis is all that can be expected. But in a few cases with at the most moderate enlargement, few signs of failure and probably a recent onset, quinidine may properly be used to try to restore sinus rhythm. When failure has been first treated with digitalis, quinidine can be given in full dosage. Conversion is usually achieved after five to seven days; if not, it is unlikely to occur and there is no purpose in continuing the drug. Fibrillation caused by thyrotoxicosis may disappear when the disease has been adequately treated by thyroidectomy or by anti-thyroid drugs. If heart failure is present, digitalis should be used as a preliminary until the thyrotoxicosis is under control. Normal rhythm will then sometimes return spontaneously. If not, quinidine can be given unless the heart shows signs of great enlargement which preclude its use. Auricular fibrillation in patients with heart disease is sometimes precipitated by some extraneous cause such as anæmia or infection, or by infarction. In these circumstances it is likely to be transitory and to disappear spontaneously, but should it persist it can generally be removed by quinidine.

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HEART DISEASE AS A CAUSE OF SUDDEN DEATH

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> 'The termination of the angina pectoris is remarkable. For, if no accidents intervene, but the disease go on to its height, the patients all suddenly fall down, and perish almost immediately'.—William Heberden in 'Commentaries on the History and Cure of Diseases', 1818.

To define sudden death precisely is difficult. Nowadays, it is usually taken to mean that death occurs within twenty-four hours (Rabson and Helpern, 1948) but there is no real time limit, and the essential feature which is implied is that the death is *unexpected*.

That death is an unpopular subject of conversation is common knowledge and there is a strong taboo surrounding the subject. Even physicians go to great pains to avoid the very word. Roget's Thesaurus lists about one hundred different expressions which may be used instead of the simple statement that the patient died! Hammann (1934) has pointed out how the very prayer from the Litany 'from sudden death, Good Lord deliver us' expresses this fear of man. Yet which of us would not be willing to forego the opportunity of a long illness, and would not prefer to slip away quickly?

The study of sudden death, especially in relation to heart disease, is of more than academic importance. First and foremost, its study shows that death is often avoidable and comes prematurely because the patient does not realize the risks he runs. This is well exemplified by coronary disease. Secondly, electrocardiographic studies at the moment of death have enabled cardiologists to formulate a line of treatment which may prevent a fatal outcome. Such examples are the prophylactic use of quinidine and procaine amide in certain cardiac arrhythmias, and the use of atropine with morphine to prevent its excessive, and sometimes fatal, vagal effect. Thirdly, the study of sudden death from the physiological aspect enables us, at least in part, to understand its mechanism. Lastly, the subject has a considerable medico-legal importance so that murder is not overlooked or people falsely accused.

PATHOLOGICAL PHYSIOLOGY

Various mechanisms have been invoked to explain the occurrence of sudden death and probably the fatal outcome results from more than one of them: spasm of the coronary arteries, the influence of powerful vagal and sympathetic reflexes, the onset of ventricular fibrillation, and cardiac standstill or asytole.

There is no doubt that both ventricular fibrillation and cardiac asystole play an important part, but which is the more common mechanism is uncertain. As long ago as 1887, McWilliam suggested that the occurrence of

ventricular fibrillation might explain sudden cardiac death in man, and since the advent of the electrocardiogram this suggestion has been amply verified both in animals and man (Clerc, 1932). Both experimentally and clinically the onset of ventricular fibrillation is preceded by extrasystoles which become profuse, bizarre and variform and arise from numerous ectopic foci (*anarchie ventriculaire*), and this leads to ventricular tachycardia which is immediately followed by ventricular fibrillation. There is no doubt that in heart block ventricular fibrillation plays an important part (Schwartz and Jezer, 1932). At first, Adams-Stokes attacks were thought to result from ventricular standstill due to a latent period which occurred before the ventricle took up its own inherent rhythm, but electrocardiograms recorded during an attack have revealed the occurrence of ventricular fibrillation in certain cases. Weiss (1940), however, is of the opinion that ventricular fibrillation plays but a minor rôle in the causation of sudden death, and he considers cardiac asystole to be much more common, sudden death being nothing more than fatal syncope.

He states that in a study of 50 cases of aortic stenosis most of the patients who suffered from attacks of syncope died instantaneously, and he believed that this, and the fact that patients suffering from the Adams-Stokes type of syncope often die instantaneously during one of their usual attacks, is evidence that the mechanisms of transient and fatal syncope are similar or identical.

The question of whether or not in sudden death ventricular fibrillation is more common than complete cardiac standstill remains unanswered.

In a paper by Stroud and Feil (1948) cardiograms taken at death in 16 cases of coronary heart disease were analysed. Of the 16 deaths 8 were due to a sudden burst of ventricular fibrillation, and 8 to sudden ventricular standstill.

Another important problem which remains unsolved is why, with the same degree of structural damage present, sudden death occurs in one person but not in another. There is no doubt that certain reflexes become hyperactive in patients with heart disease and that death can occur without further demonstrable structural change. Instantaneous death in angina pectoris is *not* usually accompanied by the formation of fresh thrombus; and often following suddenly fatal coronary occlusion, no further structural changes can be discovered at necropsy. No matter how exacting the scrutiny of the pathologist, he cannot say from examination of the heart alone that this patient died suddenly and this one did not. There is an increased irritability of the afferent or efferent cardiac nerve endings, or the central synapses, and the sensitizing factors responsible may be either transient, such as emotional or chemical, or persistent, due to a structural change. In the presence of coronary sclerosis there is a tendency to hypersensitivity of the vagal type of carotid sinus reflex. Weiss (1940) quotes a case in which this reflex became so sensitive following coronary occlusion that turning the head or gentle manipulation of the skin of the neck close to the carotid sinus induced alarming transient asystole.

Experimentally, LeRoy and Snider (1945) have demonstrated by colour film cinematography that in dogs after ligation of the left coronary artery there is a

generalized reflex coronary vasoconstriction of vagal origin which eventually kills the dog by ventricular fibrillation if it is unchecked, but that the reflex can be partially abolished by atropine. Atropine sulphate in appropriate doses reduced the mortality of their dogs by about 35 per cent.

From their work it seems clear that in man, when morphine is used for cardiac infarction, something must be done to offset its vagal action, and it is as well to give a large dose of atropine at the same time.

CLINICAL CAUSES OF SUDDEN CARDIAC DEATH

When all the causes of sudden death are considered it is surprising how often disease of the heart and aorta occurs. In the series described by Bedford (1933) cardiovascular causes amounted to 73 per cent. of the total, and of Sheldon's (1932) 443 cases of sudden death, 243 were due to heart disease. Hammann (1934) has assembled the figures of Bedford (1933), Durck (1931), and Koppisch (1934), and concludes that diseases of the cardiovascular system, including arterial embolism, thrombosis, and hæmorrhage, as a cause of sudden natural death account for 91 per cent. of cases, and of these, 65 per cent. are due to disease of the coronary arteries (including coronary occlusion from syphilitic aortitis), 21 per cent. occur with valvular heart disease, 10 per cent. with myocardial disease, and 3 per cent. with cardiac hypertrophy. More recently, Rabson and Helpern (1948) found that diseases of the heart and aorta accounted for 45 per cent. of cases of sudden death.

The following provisional classification includes most of the cardiac causes of sudden unexpected death. Often, of course, there is overlap and sometimes several causes are present—for example, some patients with angina have also aortic stenosis and yet may die from heart block. Many cardiac patients die suddenly and unexpectedly from pulmonary embolism, but usually the embolus arises from one of the deep calf or plantar veins and the cause of death is not the heart disease *per se*. However, the differential diagnosis between acute pulmonary embolism and cardiac infarction may, at times, be extremely difficult.

TABLE I

CLASSIFICATION OF CARDIAC CAUSES OF SUDDEN DEATH

(1) *Disease of the coronary arteries*
- (i) Sudden death without previous symptoms.
- (ii) Angina pectoris.
- (iii) Cardiac infarction.
- (iv) Syndromes intermediate between angina and infarction.
- (v) Coronary embolism.

(2) *Diseases of the aorta*
- (i) Syphilitic aortitis.
- (ii) Dissecting aneurysm.
- (iii) Coarctation.

(3) *Diseases of the heart valves*
- (i) Aortic stenosis.
- (ii) Aortic incompetence.
- (iii) Mitral stenosis (ball thrombus).

(4) *Diseases of the myocardium*
- (A) Carditis: (i) Diphtheria.
  (ii) Rheumatism.
  (iii) Allergy.
  (iv) Fiedler's isolated myocarditis.
- (B) Other diseases: (i) Tumours—pedunculated myxoma, rhabdomyoma.
  (ii) Sarcoidosis.

(5) *Disease of the pericardium*
- Tamponade from hæmopericardium or pericardial effusion.

(6) *Therapeutic drugs*
- Digitalis.
- Mercurial diuretics.
- Adrenaline.
- Emetine.
- Potassium.
- Chloroform.

(7) *Cardiac trauma*

CORONARY ARTERY DISEASE

Disease of the coronary tree is by far the most common and important cause of sudden unexpected natural death. If an adult apparently in perfect health suddenly falls dead, the chances are overwhelmingly in favour of coronary occlusion. As has already been pointed out, at necropsy it is not possible to say which patient died suddenly. Some patients die suddenly and others gradually, or even from other causes, and yet at post-mortem examination the lesions appear identical. There must be some other factor in the fatal case, such as the hypersensitive reflexes already referred to.

The most careful analyses recently published are those of Helpern and Rabson (1945, 1948). They give an account of sudden and unexpected natural death verified at necropsy in 2,030 consecutive cases. Diseases of the heart and aorta were first among the causes of death and accounted for 45 per cent., and the rôle of coronary arteriosclerosis in this galaxy is best illustrated by the fact that in almost one-third (30.4 per cent.) of the entire series of 2,030 cases, death was caused by that disease. Yet as recently as 1939, Hallermann in Germany found the incidence of coronary arteriosclerosis in his series of 6,481 sudden death necropsies to be only 10.5 per cent.

According to Helpern and Rabson (1945, 1948) coronary artery disease as a cause of sudden death is almost exclusively a malady of white people, and of men. Only 6 per cent. were women. Not that negroes are immune to sudden death from cardiac disease, for of their 46 cases of death attributable to obstruction of coronary ostia in syphilitic aortitis, 39 per cent. were negroes. The most fatal years were between the ages of fifty and fifty-four.

Of the 617 instances of coronary artery sclerosis, *almost three-quarters* (73.3 *per cent.*) *had no grossly demonstrable associated fresh thrombosis of the vessels.* In most cases atheroma, with or without calcification, had produced significant diminution of luminal calibre. Non-thrombotic sclerosis was

free of fibrosis in 45 per cent. and was associated with fibrosis in only 50 per cent., *whilst infarction occurred in only 5 per cent.*

It follows from the above that it is becoming increasingly important for the clinician to recognize the various atypical syndromes which betray the presence of coronary atheroma. Many cases do not fit the standard textbook descriptions of angina pectoris or cardiac infarction. In others the electrocardiographic changes are purely transient, showing either the alteration in the position of the RS-T segment referred to by Master (1946) as coronary insufficiency, or showing frank inversion of the T waves which subsequently return completely to normal, although recovery of the T wave does not necessarily imply recovery of the patient (East and Oram, 1948). If electrocardiograms are not taken early and repeatedly many of these cases will be missed.

In 10 per cent. of fatal cases of cardiac infarction death is due to rupture of the heart (myomalacia cordis), but death in these cases is not necessarily sudden, and they may live for a week or more, ultimately dying of tamponade due to a hæmopericardium.

Coronary embolism is relatively uncommon and nearly all the reported instances have been due to detachment of part of a vegetation resulting from bacterial endocarditis.

DISEASES OF THE AORTA

Syphilitic aortitis.—There is no doubt that a remarkable change has occurred in the character of syphilis over the past few decades. Florid skin lesions and gummas are uncommon now, and syphilis of the cardiovascular and central nervous systems is more important. In cardiovascular syphilis, syphilitic aortitis is almost exclusively the lesion found. This can lead to sudden death in any of four ways, namely, by the syphilitic process occluding the coronary artery ostia, by rupture of a saccular aneurysm, by the development of aortic incompetence which interferes with the filling of the coronary arteries, mainly by giving rise to a fall in the mean aortic pressure which is the main factor deciding coronary filling, and by rupture of a focal dissecting aneurysm which usually ruptures into the pericardium.

Under the stimulus of the spirochæte the vasa vasorum, which in health penetrate at most only to the outer half of the aortic media, extend through the whole media and invade the intima, producing fibrous tissue. These plaques tend to encircle the aortic ring, producing the so-called 'girdle of Venus', and the new fibrous intimal tissue invades the orifices of the coronary arteries. The occlusion may be so complete that it is difficult to distinguish the extremely narrowed lumen from the branches of the vasa vasorum that are found in the occluding tissue (Leary, 1940). Rarely, the syphilitic arteritis may extend for a short distance beyond the portion of the coronary artery within the aortic wall (Moritz, 1931). The coronary arteries in syphilitic aortitis show less atheroma than is usual at corresponding ages, perhaps because of the reduction in coronary artery pressure

by the narrowed ostia, although often a good collateral circulation develops between the aortic vasa vasorum and the pericardial vessels and bronchial arteries (Wearn, 1928). It is a hazardous circulation, however, and sudden death may result.

The syphilitic intimal tissue above the aortic ring may become necrotic and rupture, giving rise to focal dissecting aneurysms which usually produce sudden death by rupture into the pericardial sac. Owing to syphilitic scarring of the media, the typical and much more common long dissecting aneurysms resulting from Erdheim's medionecrosis are not produced.

Dissecting aneurysm.—According to Shennan (1934), about 10 per cent. of all cases of dissecting aneurysm recover from the initial attack, usually owing to the dissection rupturing back into the lumen of the aorta. Apart from such an obvious cause as external rupture, however, the dissecting aneurysm may burst into the pericardial sac, or it may involve the coronary arteries suddenly. Oram and Holt (1950) have reviewed the various ways in which the coronary arteries can be involved in dissecting aneurysm, and the more important include occlusion of the coronary ostia by the aneurysm, extension of the dissection along the coronary arteries, and compression of the coronary arteries from without by extravasated blood from the aneurysm. They believe that the electrocardiogram in these cases may show highly suggestive features.

Coarctation of the aorta.—Sudden death from rupture of the aorta, which may be hypoplastic in this disease, occurred in 19 per cent. of Maude Abbott's (1928) cases. With modern surgery, sudden death may occur on the operating table from cardiac asystole when the aorta is clamped, especially if a subclavian artery has been included in the clamp; or later from tearing out of sutures from a hypoplastic aorta distal to the constriction; or during convalescence from rupture along the suture line, owing to non-healing of the anastomosis because of superimposed infection. Sudden death may also arise in this disease from subarachnoid hæmorrhage, as in 4.5 per cent. of Abbott's cases.

OTHER CARDIAC CAUSES OF SUDDEN DEATH

Aortic valve disease.—In addition to aortic incompetence leading to sudden death, aortic stenosis alone can also cause sudden demise. Quite apart from sudden death from angina pectoris, which is present in 20 per cent. of patients with aortic stenosis (Contratto and Levine, 1937), death in this disease may result from fatal syncope. The angina pectoris appears to depend upon poor coronary filling secondary to a jet effect or to a low mean aortic pressure. The syncope of aortic stenosis is of two kinds, vasomotor and cardiac. The low blood pressure of aortic stenosis predisposes to vasomotor and orthostatic syncope. Cardiac syncope is probably due to ventricular fibrillation. De Veer (1938) considers that in some cases sudden death can be explained by the locking of a rigid but free aortic cusp against rigid fused cusps in diastole.

Myocardial disease.—Sudden death in diphtheritic myonecrosis is common and well known, although some patients die of congestive heart failure. Peripheral failure is often present in those who die suddenly. If the patient survives, complete recovery is invariable (White *et al*, 1937).

Sudden unexpected death in rheumatic carditis is most rare, and when it occurs it is probably due to the rheumatic process involving the coronary arteries. Griffith and Huntington (1946) could find only three such examples of sudden death among over 7000 cases of active rheumatic carditis.

The course and prognosis of tumours of the heart vary with the nature of the tumour, but sudden death is not uncommon even with benign tumours such as a myxoma, which need not necessarily be pedunculated, or rhabdomyoma. Sarcoidosis of the heart has caused sudden death (Kulka, 1950).

Therapeutic drugs.—Of drugs used for treatment, which can cause sudden death, digitalis is undoubtedly the best example. Buchner (1934) was the first to demonstrate that myocardial necrosis could result from its use in cats; this probably results from constriction of the coronary arteries by the vagal stimulation effect of digitalis, as it can be prevented by atropine (Kyser, Ginsberg and Gilbert, 1946). If given in sufficiently large doses in man, digitalis can induce any arrhythmia, including, finally, ventricular fibrillation.

Sudden death following intravenous diuretics probably occurs more commonly than is reported. It usually occurs in patients who have already received many injections without untoward effects, and there may be no warning. For this reason mercurial diuretics should always be given intramuscularly.

Adrenaline in large doses, especially if given intravenously by accident, may induce almost any arrhythmia except heart block, and transient hypertension and inversion of T waves are common. Occasionally the adrenaline produced by a phæochromocytoma will induce angina-like pain, and the diagnostic manœuvre of attempting to massage such a tumour to liberate adrenaline may prove most dangerous.

Emetine, until the 1939-45 war, had a bad reputation for sudden death, and it is usual to keep patients under treatment for amœbic dysentery in bed while receiving their course. In spite of a recent paper by de Cossio (1952), in which every patient treated with emetine showed inversion of the T waves in the chest leads, the danger has probably been exaggerated, and in any event, with the modern tendency to give smaller total amounts of emetine, the danger is certainly much less than was thought.

Potassium salts are occasionally employed in large doses, such as 8 to 16 g., in an attempt to stop paroxysmal tachycardia, and have been used also to differentiate inversion of the T wave due to coronary disease from other causes. The risk of sudden death is too great to permit their use for either purpose.

Cardiac trauma.—Fatal trauma to the chest over the region of the heart

may be quite trivial, and insufficient to cause any cardiac damage. Experimentally in dogs a heavy blow may bruise the heart and cause ventricular fibrillation or even cardiac rupture, and probably man reacts in a similar way (Bright and Beck, 1935).

CLINICAL ASPECTS

It will be appreciated that whatever the cause of loss of consciousness, be it cardiac asystole, ventricular asystole (Adams-Stokes attacks), ventricular fibrillation, ball valve thrombus of mitral stenosis, locking of a valve cusp in aortic stenosis, or impaction of a pedunculated myxoma, the clinical picture will be similar.

The attack occurs at any time with dramatic suddenness and without warning. The patient falls unconscious immediately, and at first is white, flaccid and pulseless, and no heart sounds are audible although he may continue to breathe. The pupils are dilated. After about fifteen seconds anoxic twitching begins and may proceed to a generalized convulsion. If the patient does not recover within three minutes, death usually results, but if recovery does ensue, return to consciousness is abrupt and complete and the patient's colour changes from white to bright red, owing to hyperoxygenated blood being suddenly pumped into a dilated vascular system (reactive hyperæmia).

Syncope due to ventricular asystole (Adams-Stokes attacks) is especially common when partial heart block becomes complete. Although opportunities to take electrocardiograms during attacks of unconsciousness are rare they are of great therapeutic, as well as diagnostic, value because some cases of Adams-Stokes attacks become unconscious as a result of paroxysmal ventricular tachycardia or fibrillation (Parkinson, Papp and Evans, 1941). If the unconsciousness is known to be due to ventricular asystole then adrenaline is indicated, but unfortunately if the unconsciousness results from paroxysmal ventricular tachycardia or fibrillation it is likely to be aggravated by the use of that drug.

Ventricular fibrillation is nearly always fatal and treatment is of little avail. Injection of 30 mg. of quinidine sulphate into the ventricle may be tried, or 5 ml. of a 2 per cent. solution of procaine hydrochloride may be injected into the auricle or may be given intravenously. In an emergency, vigorous thumping of the chest wall over the heart has occasionally been successful in abolishing the arrhythmia. If the heart stops with the patient on the operating table the immediate treatment is artificial respiration, during which time oxygen is administered by means of an anæsthetic mask. An attempt must be made to determine whether the condition is one of cardiac standstill or ventricular fibrillation. If an electrocardiogram is not immediately available the heart must be felt or seen. If fibrillation is absent, the heart is massaged, and this is easy if the thorax is open. If the abdomen only is open, the heart is massaged through the diaphragm. If this is not soon effective the left cupola is incised and the hand inserted into the

thorax from the abdomen. If neither thorax nor abdomen is open, a direct approach through the fourth or fifth intercostal space on the left side is made, to allow the index and middle fingers to do intermittent compression of the ventricle against the sterum. When it has resumed beating, 1 ml. of adrenaline may be given intramuscularly. If it does not resume beating, 1 ml. of adrenaline is given into the right auricle. If ventricular fibrillation is seen or felt, defibrillation must be achieved before cardiac massage is attempted. Quinidine sulphate and procaine hydrochloride are used as described on page 27.

If the risk of ventricular fibrillation or paroxysmal ventricular tachycardia is great, for example, following cardiac infarction or in status anginosus, quinidine sulphate, 3 to 5 grains (0.2 to 0.3 g.) thrice daily, orally, or procaine amide ('pronestyl' Squibb), 0.5 to 1 g. thrice daily, may be used prophylactically.

It is apparent that a person threatened with sudden loss of consciousness should not undertake any activity which might endanger himself or others should a sudden unexpected attack occur.

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THE SURGERY OF THE HEART AND GREAT VESSELS

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A PATENT ductus arteriosus was first tied by Gross in 1939. When we consider the number of operations performed on the heart and great vessels today, we realize how rapidly surgery has advanced in the treatment of conditions which a few years ago aroused little more than an academic interest; and because the scope of cardiac surgery is as yet limited to a few conditions we can only guess at the extent of its development. Nevertheless, we can be sure that further progress will be made and that there is hope for other forms of heart disease for which as yet we have found no remedy.

THE BASIS OF CARDIAC SURGERY

Modern cardiac surgery is based on three observations:—

(1) Large vascular channels can be occluded by ligature or suture.

(2) Anastomoses can be established between large blood vessels.

(3) The heart itself can be incised so as to permit the introduction of instruments and the wound so made safely sutured.

The first point is no novelty and has been recognized for many years, but the two latter points have been solved only recently. It is indeed remarkable that blood vessels, sewn together with sutures of almost infinitesimal fineness, stay united and act as patent living tubes as readily as other visceral canals. Incision into the chamber of the heart has become straightforward now that it has been established that the heart should not be displaced and that anæsthetic agents such as procaine reduce its irritability during manipulation. Hæmorrhage can be controlled by digital pressure or light clamps, and simple sutures suffice to repair the wound in the heart muscle.

The knowledge that cardiac surgery is available makes it imperative that diagnosis and assessment are complete and accurate. Clinical and radiological methods usually give adequate information for diagnosis, but the surgeon wants to know a great deal more about the degree and extent of an abnormality on which he proposes to operate. For this reason two additional methods of investigation are now often used; certainly in any case in which information can be found that could not otherwise be supplied. These are (i) cardiac catheterization, and (ii) angiocardiography.

Cardiac catheterization consists in passing a very fine polythene catheter through an arm vein into the superior vena cava, thence to the right auricle, ventricle and pulmonary arteries. The catheter tip is followed under the x-ray screen and records are made of the pressure changes. Samples of blood can be taken for estimation of the oxygen and carbon dioxide content. If, for example, the catheter after passing into the right auricle and right

ventricle suddenly appears in the aorta instead of the pulmonary artery, the presence of an interventricular septal defect can be inferred. Passing the catheter out through the pulmonary artery into the lung field will also give important information.

Angiocardiography consists in injecting at very high speed a quantity of radio-opaque solution into the circulation (diodone, 70 per cent., 50 to 100 ml. as an average). Skiagrams are taken as quickly as possible so as to watch the course of the dye as it flows along the veins into the heart. Special apparatus is required to take the six or seven films that have to be exposed within two or three seconds of the injection. From these almost cinematographic pictures the progress of the dye can be observed and the interior of the heart outline made out. These methods are additional to the ordinary accepted clinical and radiological investigations and do not replace them; nor are they necessary in every case.

INDICATIONS FOR CARDIAC SURGERY

The customary division of heart lesions into congenital and acquired has certain applications to surgery: for example, in the congenital group the heart muscle is normal and the defects are mechanical ones of stenoses or fistulæ, whilst in acquired lesions pathological changes have not only produced valvular damage but have also affected the myocardium. The congenital conditions require treatment when the victims are young, or at any rate at a much earlier age than in acquired heart disease. Patent ductus arteriosus, pulmonary stenosis and coarctation are accepted examples of congenital disease suitable for treatment, and mitral stenosis is the most important acquired lesion in this respect. In both groups there are other conditions which have been operated on and which may be suitable for surgery at some future date, but in this article discussion will be confined to these four examples.

Congenital heart disease.—In congenital heart disease it is convenient to consider the features of patent ductus and pulmonary stenosis together, because they are almost opposites, a position which can best be summarized as shown in table 1.

PATENT DUCTUS ARTERIOSUS

It is well known that some cases of patent ductus can survive into adult life. The case for surgical intervention is based on the knowledge that adult survivors are not common and that many patients who pass through their childhood with little disability encounter the effects of the added load on the left heart in early adult life. In other words, heart failure will occur if the amount of blood lost through the fistula from the aorta cannot easily be compensated for by the left ventricle. Another complication, fatal before the era of penicillin, is infective endocarditis, and although this responds to antibiotics, pathological changes invariably follow the healing process. A

third and important factor is the cardiac invalidism that is thrust on the children by doctors, students, parents and school teachers. Once a child is known to have an abnormal heart he is never allowed the freedom accorded to a normal child, and not unnaturally becomes introspective as well as physically restricted. In brief, we feel that surgery should be considered in

TABLE I

	Patent Ductus	Pulmonary Stenosis (Fallot's tetralogy)
The lesion	A fistula (left to right) Excessive blood flow through lungs Uncomplicated Left ventricular enlargement	A stenosis Inadequate pulmonary circulation Complicated (e.g. patent interventricular septum overriding aorta) Right ventricular enlargement
Treatment	Closure of the fistula	Construction of a fistula or opening the stenosis
Clinical features	Normal colour, *white* Normal exercise tolerance and activities Normal fingers Socially normal Mentally normal Continuous machinery (systolic and diastolic) murmur Increased pulse pressure Normal blood count	Cyanosed, *blue* Dyspnœa on exertion with limitation of activities Clubbing of fingers and toes Difficult and a burden to family Variable—irritable, but often intelligent Systolic thrill and murmur over pulmonary area Normal or low blood pressure Polycythæmia: Hæmoglobin, 125 to 170 per cent. Hb. R.b.c.'s 6 to 7½ million
Radiological features	Long chest with globular heart Bulging pulmonary conus Left ventricular enlargement Increased pulmonary vascular markings with vigorous pulsation (Hilar dance)	Short square chest with 'sabot' shaped heart (apex tipped counterclockwise) Concavity in pulmonary artery area Right heart enlargement Deficient vessel markings in the lung fields with absent pulsations

every child over the age of four or five years with an uncomplicated patent ductus, so that they can face their school days as normal children after the ductus is tied. This is not to say that there is not a number of cases in which surgery does not seem called for; these can be observed expectantly over a period of years.

If an active policy is to be accepted it must promise good results with a low risk rate: this is what can be achieved. The mortality in large series of cases is in the neighbourhood of one or two per cent., and the complications are rare. What is significant is that once the operation has been performed the recovery is quick. A child is usually home in ten to fourteen days, takes up normal existence and appears to forget about the disability altogether. Moreover, if there has been enlargement of the heart, this is often reduced within a week or two of operation.

From the technical point of view the operation consists of exposing the ductus as it lies under the arch of the aorta and, after dissecting it free, ligating it with strong material or dividing the canal and suturing the cut ends. It is a straightforward procedure, but no surgeon will ignore the dangers of massive hæmorrhage if the ductus or either of the adjoining channels is in any way injured.

PULMONARY STENOSIS (FALLOT'S TETRALOGY)

Cyanosis and shortness of breath are the dominant features in this class of case. The blueness dates from birth or shortly after; the dyspnœa may only become apparent as the baby or child starts to exert himself or herself, but becomes increasingly obvious and crippling as the years go by. The obstruction in the pulmonary outflow tract prevents an adequate circulation of blood through the lungs. Gross pulmonary stenosis is incompatible with life unless there is some shunt between the pulmonary and systemic circulations. A patent ductus or a patent intracardiac septum affords such a safety valve, but in Fallot's tetralogy, which is the most common and surgically the most important example of this group, the complicating factors are a patent interventricular septum and an overriding aorta. The aorta therefore receives blood from the right ventricle as well as the left; in other words, venous blood enters directly into the systemic circulation. The cyanosis is therefore due to a combination of an inefficient pulmonary flow and a systemic circulation of mixed venous and oxygenated blood. To compensate for the low oxygen content of the arterial blood a polycythæmia develops and the blood hæmoglobin may be 50 or even 100 per cent. greater than normal.

Apart from the obvious disability and blueness, these children are a heavy burden on their families, who devote an excessive amount of attention to these little sufferers. Other clinical points of importance are clubbing of the fingers and toes and liability to coughs and colds, and sometimes the presence of other abnormalities. Although these children may have cerebral congestion producing irritability, they are not necessarily stupid. There are all types of variations in severity of the symptoms. Children may have been blue from birth and may be practically unable to walk, always squatting whenever possible. At the other extreme they show inability to undertake heavy exercise, but may otherwise lead a more or less normal life into early adult age. But no matter how apparently slight the disability, any relief is welcome.

Operative treatment of this condition dates from the brilliant and ingenious anastomotic operation introduced by Blalock and Taussig, who followed the principle that part of the systemic arterial blood should be directed into the pulmonary field. In practice, the Blalock type of operation consists in anastomosing the divided subclavian artery into the side of the corresponding main pulmonary artery. This artificial ductus, which is

fortunately of the right size to give improvement but not so large as to produce an excessive load on the left ventricle, undoubtedly gives considerable relief of symptoms and of colour. It is not, however, a cure. It is

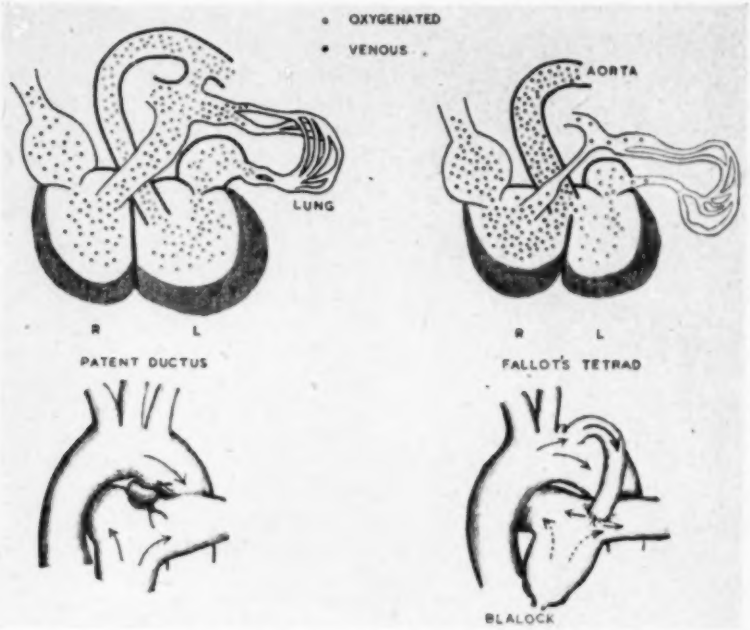

FIG. 1.—Diagrams to illustrate the essential differences between a patent ductus arteriosus and pulmonary stenosis with Fallot's tetralogy. In the ductus, oxygenated blood from the left heart can pass into the pulmonary artery and there is no question of failure of oxygenation of blood in the lungs. In the Fallot only a limited amount of venous blood reaches the lungs and a considerable quantity enters the aorta direct from the right ventricle through the agency of the patent interventricular septum. The lower diagrams indicate the methods of treatment, the ductus being closed by ligature or division and suture, and the Fallot by making an artificial ductus (Blalock's operation). Potts' operation is on similar principles to that of Blalock, but the anastomosis is made direct between the aorta and the left pulmonary artery.

in effect a further disability to add to the already complicated state of the heart, but the fact remains that the benefit given by the operation is remarkable: it will allow children, who previously have had to be wheeled about, to play a certain amount of games, to bicycle and to lead a normal school

life. Potts' operation, a modification of the above principle, consists in making an anastomosis between the side of the aorta and left pulmonary artery.

In addition to this indirect form of operation, there is a direct attack on the stenosis. It is undoubtedly the correct operation in cases of pure pulmonary stenosis (as distinct from Fallot's tetralogy), and here the distorted and stenosed pulmonary valve is split with a valvotome, introduced into the right ventricle, as suggested by Brock and myself. Brock has further developed the operation of pulmonary valvotomy into a punch-resection of the stenotic area, if this has been shown to be of a suitable size and shape for this procedure. In these operations the instrument is introduced through a small incision in the anterior wall of the right ventricle, and directed against the narrowed area. The suture of the incision in the heart muscle does not present many technical difficulties and there is usually little loss of blood, even though several instruments may have been used.

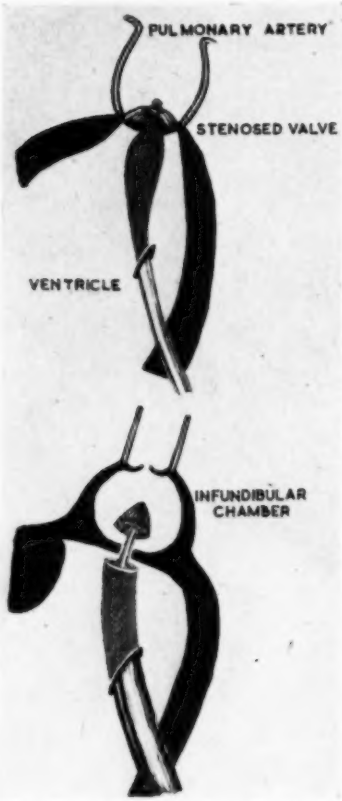

FIG. 2.—*Pulmonary stenosis.* — Direct operation. Upper diagram indicates methods of using valvotome for a stenosed pulmonary valve. Lower drawing indicates how a punch can be used to resect the septum between the ventricle and an infundibular chamber (Brock's operation).

There has not been time enough to decide if one operation is better than the other, but probably each has its place, and the actual procedure need not be determined until the heart is exposed at operation and the nature of the stenosis directly studied.

In the hands of the experienced cardiac surgeon the mortality in these 'blue baby' operations is between 7 and 8 per cent. Most surgeons admit to finding that their early results have been greatly improved upon as time progresses. The complications, fortunately, are comparatively few and far between. In practically every case some benefit is obtained; sometimes this is dramatic and these patients will be embarrassingly grateful for what is not a curative operation. If one operation fails

to give improvement there is a chance that something can be done on the opposite side; alternatively, if the indirect operation has been performed first, the direct one can be used at a later date.

COARCTATION OF THE AORTA

Coarctation of the aorta in its most simple and common form is a transverse stricture of the aorta situated at the level of the ductus arteriosus. The opening may be only 2 to 3 mm. in diameter, with the result that the blood flow below this point is inadequate. Clinically this is gauged by palpation of the femoral artery which is pulseless, and many diagnoses have

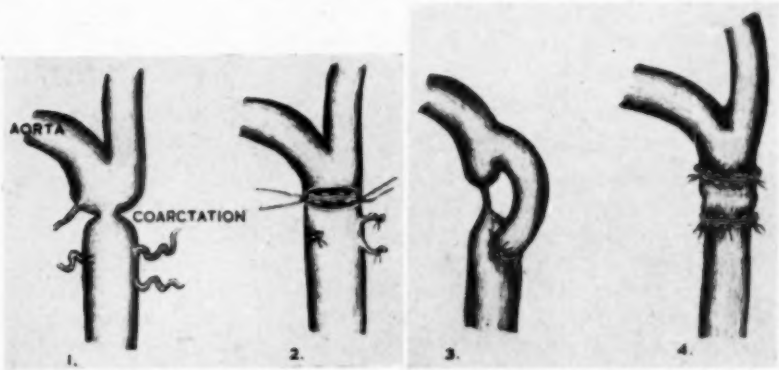

FIG. 3.—(1) *Coarctation* of the aorta with possible operations. (2) End-to-end junction after resection. (3) Subclavian artery turned down to descending aorta. (4) Use of aortic graft.

been established by recalling this simple observation. The reduced blood flow is deleterious to renal function which is an important factor in leading to cardiac enlargement and hypertension above the stricture. Above the level of the coarctation this hypertension steadily increases and a brachial blood pressure of considerable height will be recorded with associated discomforts in the form of throbbing headaches, giddiness and misty vision, which may be the first actual symptoms of the disease. To maintain some form of blood supply to the tissues below the stricture large compensatory anastomoses develop between the hyper- and hypo-tensive fields. Clinically these arteries are palpable in the posterior scapular areas, and the dilated and tortuous intercostal arteries may actually erode the lower borders of the ribs and produce radiologically detectable notching.

The onset of hypertension may pass unnoticed in a child unless for any reason the blood pressure is taken, or the absence of femoral pulses is noted. When symptoms develop, which they may do about adolescence or early adult life, the probability is that atheromatous change will have occurred in the great vessels. Few patients survive into middle age.

The mechanical problem to be solved by surgery is that of a stricture. If this is limited in extent it can be excised and the cut ends of the aorta sutured together as suggested by Crafoord and by Gross. If the ends cannot be brought together the large left subclavian artery can be divided and turned down, and used to bridge a limited gap. In other cases a free aortic graft has been employed to fill the deficiency. The success of the operation depends upon the ability to suture the ends of the aorta, for, if there are atheromatous changes, the risk of torn-out stitches and failure to obtain a 'blood-tight' junction are considerable. Consequently, the younger the patient the more successful the operation is likely to be, and most surgeons now regard twenty years as the upper limit and prefer to operate between the ages of seven and fourteen years, when there are few or no symptoms and when the vessel walls are healthy. The problem is to diagnose the condition at this stage, and to justify to the parents the necessity for a major operation in a child who is apparently fit.

MITRAL STENOSIS

Of all acquired heart lesions, mitral stenosis is the only one which has as yet proved amenable to surgical treatment. This end-result of rheumatic fever has previously been regarded as only part and parcel of a generalized rheumatic carditis, and until recently the teaching has been that there would be little advantage in improving the stenosis because the heart muscle was already so damaged. This has not proved to be the case, and during the past few years a number of patients with mitral stenosis have been operated on successfully and with marked relief of their symptoms. In fact, the present operation, as regards the early results at any rate, has been one of the most dramatic achievements in present-day surgery. Grossly dyspnœic patients, unable to lie down or walk more than a few steps, have sometimes been able to return to activities that can be judged by climbing two flights of stairs without breathlessness and doing all the housework.

If surgery is to be considered, the most important criterion is that the rheumatic process in the heart should be as quiescent as possible; in other words, the interval between the end of the active stage of the disease and operation should be as long as possible. It is also more satisfactory to operate when the patient is young, when the heart is small and not enlarged, when the rhythm is regular, and when the symptoms are not very marked. It is rare for all of these conditions to be found, and the majority of patients selected as suitable for surgery fail to live up to the criteria suggested. On the other hand, it is important that gross congestive failure should not be present even though recurrent attacks of pulmonary œdema stress the urgent need for operation. If the heart is fibrillating, the risk of thrombus formation within the auricles is present, and this is an added risk of surgery since such a clot may easily be converted into an embolus during the manipulations of operation. There are numerous investigations and methods of assessment

which all help to build up a picture which gives some idea of the severity of the stenosis, but with most stenoses there is a certain amount of regurgitation, and if it is thought that surgery will exaggerate this reflux, then it may be considered that operation will do more harm than good.

The operation itself consists in splitting the fused cusps along the line where they have become adherent. These lines of fusion are referred to as the commissures, and in a satisfactory operation these are split from the stenotic opening outwards in an antero-lateral and postero-medial direction

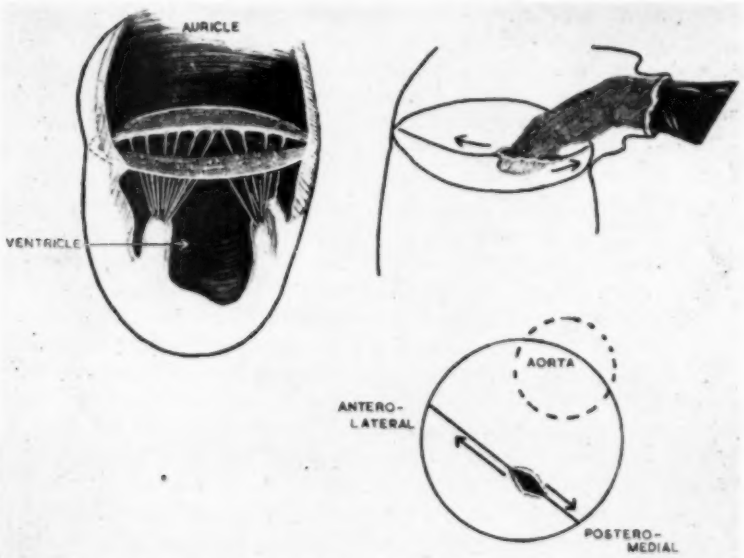

FIG. 4.—Diagram to illustrate the principle of *mitral valvotomy*. Diagram on the left shows the arrangement of the valve leaves with their chordæ tendineæ. The finger introduced into the auricular appendix aims to split the fused commissures along the lines of fusion and thus to reproduce so far as possible the valve flaps.

to the valve ring, so that two flaps approximating the normal condition are formed. If these valve flaps are not distorted or drawn down by shortening of the chordæ tendineæ a very fair approximation of normal valve action is reproduced, and it seems probable that the torn raw edges produced by the splitting become readily endothelialized and, in the absence of further rheumatic infection, heal over.

The approach to the valve that is now accepted is through the left auricular appendix, particularly if this is large. The operation consists of a wide thoracotomy (at the present time we tend to use a fifth-rib postero-lateral incision), and then to open the pericardium freely. A large, tense and engorged

pulmonary artery and pulmonary veins will be seen, whilst the enlarged auricular appendix protrudes forward in the region of the auriculo-ventricular groove. A clamp is placed on this appendix and the tip cut away to leave an opening one-and-a-half times the diameter of the index finger. The right index finger is then inserted into this opening and, as the clamp is released, advanced into the cavity of the auricle. The tip of the finger is passed forward and downwards to reach the curved valve area where the rough edges of the stenotic opening can be palpated; so long as the opening is not obstructed for any length of time the finger is well tolerated.

After orientating the lines of the commissures the side of the finger is used to rupture the fused valve cusps. It may be difficult to start this tearing movement, but once it has been started the remainder of the commissure splits easily. The operation is thus not a dilatation but an incision, although one that is done blindly and possibly a little crudely. Areas of calcification and strong fibrosis may make the finger useless as an operating instrument, and attempts can be made with a variety of knife blades and steel finger nails applied to the exploring digit to improve its utility. When the operation is complete (and this may take only a matter of seconds, although with difficult cases up to five or ten minutes may be required), the finger is withdrawn and the clamp re-applied. The cut end of the auricle appendix is sutured, and if there is no leaking the operation is completed. The loss of blood is usually slight, though there are the obvious dangers of hæmorrhage if any tearing or damage occurs to the auricle wall; if bleeding does occur it is not simply a case of a brisk hæmorrhage, it is one of a blood bath which requires considerable activity and dexterity to control.

After operation, recovery is usually good and rapid if the valve splitting has been complete and successful; if a valve leaf itself has been torn, particularly the aortic cusp, the risk of regurgitation and consequent extra load on the circulation is considerable. Emboli detached from the left auricle may produce hemiplegia, aphasia and other phenomena in the systemic circulation. Emboli can also be discharged from the right auricle by the improved circulation and lead to pulmonary infarction of varying severity. The operation risk is low, indeed lower than might have been expected. We have had no deaths in more than fifty of these operations.

The success of a good commissurotomy is sometimes dramatic—a bedridden, dyspnœic and blue patient can, within two to three months, climb stairs, push a pram, and do her own heavy housework. Other cases recover more slowly and less satisfactorily, particularly those with considerable pulmonary hypertension over a prolonged period, but some improvement is obtained in every case in which the stenosis has been improved, even though not to its full extent. The risk of recurrence is felt to be appreciable if the rheumatic process was not quiescent at the time of operation or if it recurs, otherwise it does not seem to be significant. Admittedly only a few years have elapsed since the operation became common practice, but the improvement

seems to be well maintained and relapses have not so far been encountered.

The magnitude of the problem as it affects the assessment and surgical treatment of patients is formidable. Even if only a small proportion of sufferers are considered eligible for operation the numbers may well occupy the activities of a number of surgeons for a long time to come. Certainly this one operation will provide more work than the rest of cardiac surgery put together if the early results continue to live up to expectation.

CONCLUSION

Consideration of the treatment of a number of other valvular and septal lesions is being actively pursued and may be available on the 'production line' any time in the near future, but the greater problem of coronary disease has not come near solution. To restore the damaged arteries is impossible, but the grafting of an additional blood supply on to the damaged heart muscle may prove of value in prolonging the vitality of any area of potential infarction.

The artificial heart-lung apparatus for excluding the heart from the patient's circulation during operation is engaging considerable attention, but with the ill and disabled patients who require surgery the setting up of the apparatus as a preliminary to the actual operation is almost too severe an additional strain to be withstood.

Cardiac surgery started in a fog of complexity which gradually thinned out with the recognition of certain principles and the development of the team to investigate and deal with the problems. The anæsthetist deserves a large amount of credit for having provided a technique which allows of wide transthoracic exposure, and using drugs which reduce the irritability of the heart to a minimum. The heart is a tolerant organ in that it puts up with many manipulations which were once considered disastrous to its function, but it still retains its sense of temperament and the unexpected. Arrhythmias and sudden arrest are complications which may occur at any time during the operation and may be extremely difficult to combat. These are in addition to the technical problems that face the surgeon in the actual performance of the operation.

THE PRACTICAL VALUE OF CARDIAC CATHETERIZATION

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When Forssmann, in 1929, by repeated cardiac catherization upon himself, showed that the procedure was not only possible, but apparently without undue danger, a new era in cardiovascular investigation began.

After some efforts by Portuguese and French investigators to use the method for outlining the heart by radio-opaque injections, the technique was developed by Cournand and Ranges (1941) for estimating cardiac output. By introducing a radio-opaque ureteric catheter into the right auricle *via* an antecubital vein, a sample of mixed venous blood could be obtained. Hitherto, measurement of the cardiac output by the Fick principle:—

$$\text{Cardiac output (litres/minute)} = \frac{\text{Oxygen consumption in ml./min.} \times 100}{\text{Oxygen saturation of arterial blood* minus oxygen saturation of mixed venous blood}}$$

was laborious, because of the difficulties of measuring the arteriovenous oxygen difference by respiratory techniques. Right auricular catheterization not only permitted an accurate estimation of cardiac output, but allowed serial observations to be recorded over a period of time, and the effect of exercise and of drugs upon the output to be assessed. From this work has stemmed the study of the function of the damaged and failing heart and its response to therapy.

There can be no doubt that the modern understanding and concepts of hæmodynamics and the rational approach to cardiac therapeutics are due largely to the introduction of cardiac catheterization. The purpose of this article, however, is to indicate how cardiac catheterization at the present time is contributing, not only to the further knowledge of cardiovascular disease, but also to accuracy in diagnosis and improvement in treatment.

CONGESTIVE CARDIAC FAILURE AND THE ACTION OF DRUGS UPON THE HEART

Initially, the study of cardiac failure was based upon measurements of cardiac output, the right auricle only being catheterized. The recognition of two main types of congestive failure, one with a low output, seen in ischæmic, hypertensive, and valvular disease, and the other with an increased output, seen in thyrotoxicosis, anæmia, and pulmonary heart disease,

*Arterial blood obtained by puncture of a superficial artery, or arterial saturation assumed normal.

was a major advance (McMichael, 1946; Stead *et al.*, 1948). These workers showed that, within certain limits, an increase in venous pressure might possibly be a beneficial, compensatory mechanism, which increased the cardiac output according to the demand, but that, beyond these limits, further increase in venous pressure was accompanied by a fall in output. Venesection was followed by an increase in output when this was initially low (Howarth *et al.*, 1946a).

The practice of passing the catheter into the right ventricle and pul-

FIG. 1.—Cardiac catheter in right pulmonary artery.

monary artery (fig. 1), and of recording not merely 'mean' pressures with a saline manometer, but also systolic and diastolic values by optical methods, using sensitive electrical manometers, has permitted more extensive and detailed study of pressure changes in the diseased and failing heart (Bloomfield *et al.*, 1946). The right auricular mean pressure (filling pressure of the heart) roughly approximates to right ventricular pressure at the end of diastole, and the systolic pressure in the right ventricle is equal to that in the pulmonary artery. Systolic pressures in the right ventricle and pulmonary artery are almost always raised in cardiac failure, either as a result of vascular disease of the lungs which increases the resistance of the pulmonary vascular bed, or of an increased pulmonary venous and left auricular pressure, such as occurs in mitral stenosis and left ventricular failure.

Digitalis, apart from its action in slowing the ventricle, stimulates the myocardium in left ventricular failure, increasing the strength of contraction. The ventricle therefore empties more efficiently, cardiac output increases, the pulmonary venous pressure is reduced, and the pulmonary artery and right ventricular pressures fall (Bayliss *et al.*, 1950b).

The action of digitalis, as well as that of theophylline-ethylenediamine and other drugs used in heart failure, has been fully reviewed by McMichael (1950). More recent work shows that cardiac failure cannot be gauged by output alone (which is the result of many factors) and which, even though high, may be inadequate for the demands of the circulation at that time. When a raised output is maintained at the expense of high vascular pressures in the lungs and systemic veins, deleterious consequences often occur (McMichael, 1952).

Studies on heart failure of pulmonary origin show that cases can be divided into obstructive and asphyxial types (McMichael, 1950), the former type being associated with a low cardiac output. The asphyxial type, as exemplified by emphysema, initially has a high output, shown clinically by warm extremities and a bounding pulse, and produced by the demand of the tissues for more oxygen. The pulmonary artery pressure rises during exacerbations of bronchitis when the arterial oxygen saturation falls (McMichael, 1948; Mounsey *et al.*, 1952). The work of Motley *et al.* (1947) showed that reduction in the oxygen content of inspired air could produce an increase in pulmonary artery pressure without an increase in output. In patients with pulmonary heart disease this increase in pressure can produce right ventricular failure, indicating the importance of carrying out every possible measure to correct asphyxia in the treatment of congestive cardiac failure due to chronic bronchitis and emphysema. Howarth *et al.* (1946b) found that when the cardiac output was elevated in pulmonary heart failure, digitalis reduced the venous pressure without increasing the cardiac output. Ferrer *et al.* (1950) showed a small increase in output but, in a further series of observations, Mounsey *et al.* (1952) found the change in output to be insignificant. There was, however, a slight increase in right ventricular pulse pressure, although it would appear that the strengthened right ventricle was unable to force more blood through the resistant pulmonary vessels. In the low output phase which succeeds the high output period, digitalis may be of value, but often at this stage the heart failure is irreversible.

As a result of cardiac catheterization and other studies, however, it is generally agreed that correction of asphyxia and control of the pulmonary infection are important factors in the therapy of congestive failure due to pulmonary disease. Oxygen, however, should be administered with care (Davies and Mackinnon, 1949).

Recently, the cardiac actions of the new hypotensive ganglion-blocking agents, such as hexamethonium bromide, upon the heart, have been investigated by means of the cardiac catheter. Werkö *et al.* (1951) have shown

that the drug causes a fall in pulmonary vascular resistance and pulmonary artery pressure. Hexamethonium may thus prove valuable in the treatment of acute left ventricular failure of hypertensive origin.

MITRAL VALVE DISEASE

The striking success of mitral valvulotomy has focused attention upon the hæmodynamics of mitral stenosis. The assessment of patients for operation, although resting mainly on clinical grounds, calls for thorough evaluation of the cardiac function in many cases. An increase in the pulmonary artery and right ventricular pressures (fig. 2) is common in mitral stenosis (Harken *et al.*, 1948; Bayliss *et al.*, 1950a), and the response to exercise differs from that in normal persons. By means of exercising the patient with the cardiac

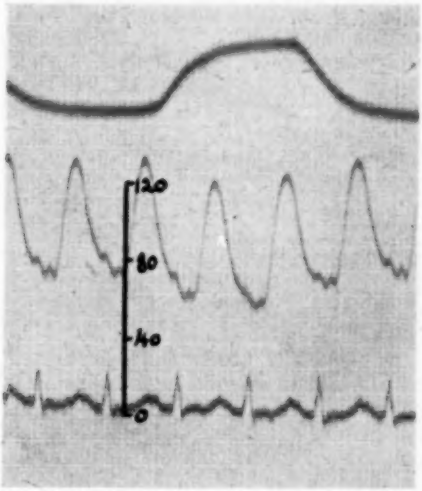

FIG. 2.—Pressure record from the pulmonary artery at rest in a patient with advanced mitral stenosis and severe physical incapacity. The pulmonary artery pressure is grossly raised above the maximum normal figure of 30/5 mm. Hg. This patient improved considerably after mitral valvulotomy. (Reference point for pressures: 5 cm. below sternal angle. Strain gauge recording.)

catheter in the pulmonary artery, Hickam and Cargill (1948) have shown that the pulmonary artery pressure rises (fig. 3). In moderately severe cases this is accompanied by a rise in cardiac output, but in severe mitral stenosis the output may show no rise or even a fall. This is the reverse of the findings in normal persons, in whom the output rises but the pulmonary artery pressure remains unaltered. This rise in pulmonary artery pressure might be the

result of the increased pulmonary venous pressure due to the mechanical obstruction offered by the stenosed valve, but other factors may also be responsible. The 'pulmonary capillary venous pressure' was measured in mitral valve disease by Lagerlöf and Werkö (1949), and by Gorlin *et al.* (1951) by passing the catheter down the pulmonary arterial tree until the

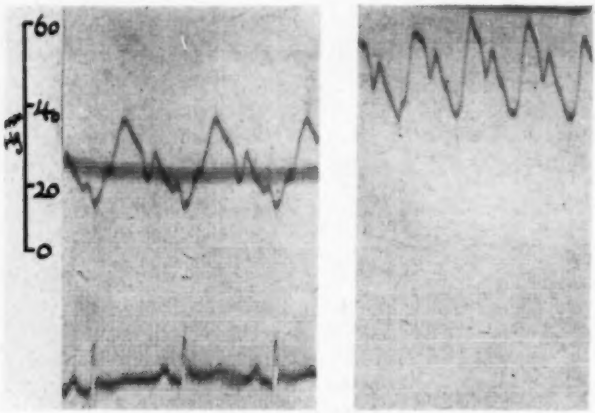

FIG. 3.—The response to exercise in mitral stenosis of moderate severity. The pressure records are taken from the pulmonary artery, the resting pressure being only slightly above the maximum normal of 30/5 mm. Hg. After exercise, the pressure rises sharply, as does the cardiac rate. The cardiac output, which is normal at rest, is nearly doubled on exercise. (Reference point for pressures: 5 cm. below sternal angle. Strain gauge recording.)

tip obstructed a small branch. In this way, the pulse wave of the pulmonary venous system, which corresponds to the left auricular pressure, can be measured (Cournand *et al.*, 1947). Dexter *et al.* (1950) have shown that in severe mitral stenosis the pulmonary artery pressure may be increased greatly out of proportion to the pulmonary venous pressure, indicating an increase in resistance in the pulmonary arteriolar bed, due either to spasm and/or occlusive changes in the arterioles. The gradient, pulmonary artery to pulmonary vein, is not, however, increased in milder cases. Further study will determine whether better results are to be expected from cases operated upon before the gradient has increased than in those with a high gradient.

Interpretation of the pulmonary capillary venous pressure curve is not always easy. The influence of the bronchial circulation is uncertain and artefacts in the tracing may occur, but in spite of these difficulties, the effects of valvulotomy on the pulmonary-artery-to-pulmonary-vein gradient will be of great interest and should also assist in determining the optimum time for operation. Furthermore, a study of the pulmonary capillary venous pressure curves in mitral valve disease may show evidence of mitral incompetence.

Clearly, an exact knowledge of the degree of incompetence present is of great value to the surgeon in determining the indications for operation and the type of operation required.

CONGENITAL HEART DISEASE

As in mitral valve disease, the advent of cardiac surgery has provided a tremendous impetus to the study of congenital heart disease. The knowledge gained by the cardiac catheter, together with that obtained by angiocardiography, now permits a high degree of accuracy in diagnosis, which

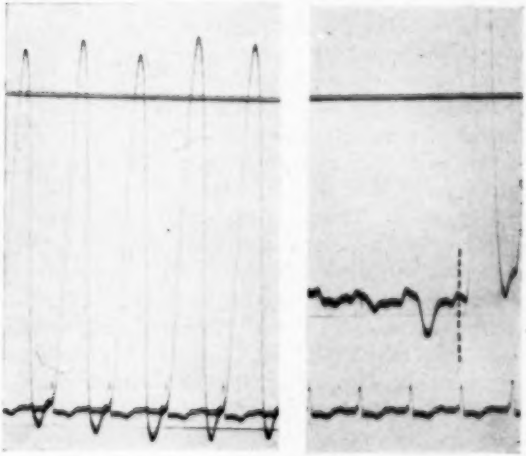

FIG. 4a.—Right valvular and pulmonary artery pressures in a case of congenital isolated pulmonary valvular stenosis. The right ventricular systolic pressure is grossly raised.
Right ventricular pressure = $\frac{132}{5}$ mm. Hg.
Pulmonary artery pressure = $\frac{27}{0}$ mm. Hg.

in turn has resulted in striking surgical successes. By means of thorough cardiac exploration with the catheter, samples of blood may be obtained from the superior vena cava, right auricle, right ventricle, pulmonary artery, and, in cases of septal defect, from the left auricle or left ventricle. When blood passes from the left side of the heart to the right (e.g., through an interatrial communication), the highly oxygenated blood can be recognized: a right auricular sample will thus have a significantly higher oxygen content than blood in the superior vena cava. Estimation of intracardiac pressures enables a diagnosis of pulmonary stenosis to be made with certainty, and provides accurate information regarding the site and the degree of severity. Fig. 4a shows the results obtained in a case of pulmonary valvular stenosis without aortic override. The pressure in the pulmonary artery is reduced, but a sudden increase occurs as the catheter is withdrawn through the

stenosed pulmonary valve into the right ventricle, which has hypertrophied in order to force blood through the obstruction. This patient, a boy of twelve years, severely disabled, was markedly improved by pulmonary valvulotomy. Fig. 4b shows an elevated right auricular pressure and a large presystolic auricular 'a' wave in the same patient. Abrahams and Wood (1951) have shown that this large auricular 'a' wave is a constant finding in severe degrees of pulmonary stenosis without overriding of the aorta. The large 'a' wave is due to increase in the end diastolic pressure of the right ventricle. The detection of a large, or 'giant' 'a' wave is a simple matter clinically, and the cardiac catheter has been of great value in elucidating the mechanism and emphasizing the importance of a physical sign which had been noted by earlier workers. Such an 'a' wave may be seen in severe pulmonary arterial hypertension, and in tricuspid stenosis, but in both these conditions the systolic pressure in the pulmonary artery is equal to that in the right ventricle, whereas in pulmonary stenosis it is lower.

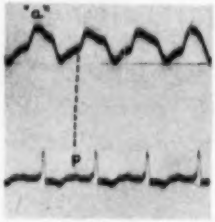

FIG. 4b.—Presystolic 'a' wave from the right auricle in the same case. (Reference point for pressures: 5 cm. below sternal angle. Strain gauge recordings.) Right auricular mean pressure = 6.8 mm. Hg.

By utilizing the Fick principle, the pulmonary artery blood flow (which is increased in malformations which produce a left to right 'shunt' of blood and decreased in cases with a right to left shunt) may be calculated, and the volume of the shunt estimated (Bing *et al.*, 1950; Cournand *et al.*, 1949; Holling and Zak, 1950). By obtaining pressure records from the right auricle, left auricle and pulmonary veins in a case of atrioseptal defect, Cournand *et al.* (1947) showed that the pressure in the left auricle was higher than in the right auricle and that the pulse curve differed in detail. Lagerlöf and Werkö (1949) have shown that pulmonary capillary venous pressure curves resemble those of left auricular pressure curves, a finding of some importance in mitral stenosis.

Wood (1950) has reclassified congenital heart disease on the basis of the findings obtained from cardiac catheterization and other investigations, and has thus emphasized the importance of physical signs and functional pathology.

Cardiac catheterization, however, does not yield certain important information regarding structural pathology, which can be more satisfactorily obtained by angiocardiography. In cyanotic congenital heart disease the latter procedure is more generally valuable, especially to the surgeon. In coarctation of the aorta, cardiac catheterization has no place, unless additional abnormalities are suspected, although catheterization of the aorta for the purpose of outlining the coarctation with contrast medium (thoracic aortography) is a recognized procedure of considerable surgical importance (Jonsson and Broden, 1950).

DANGERS OF CARDIAC CATHETERIZATION

Catheterization of the right auricle carries no more risk than an intravenous infusion. Occasionally, local venous thrombosis occurs at the site of introduction of the catheter, but this is exceptional if correct technique is observed. When the catheter is advanced beyond the tricuspid valve, ectopic contractions are usual, and there is a risk of a serious, or even fatal, arrhythmia, especially in severely damaged hearts. In most cases, this risk is very small, even in the presence of cardiac failure, but patients with very large hearts, ischæmic heart disease, and severe cyanotic congenital heart disease present greater hazards. The tendency to arrhythmia can be reduced by the use of quinidine or procaine amide by mouth before the procedure, or by procaine amide injected through the catheter, and by adjusting the tip of the catheter if ectopic beats become numerous. The tricuspid region and the outflow tract of the right ventricle are the most usual sites at which ectopic rhythms are elicited, the pulmonary artery being much less sensitive. Embolism as a result of small thrombi on the catheter tip is rare if a constant drip of heparinized saline is maintained, although in polycythæmic patients with cyanotic congenital heart disease this complication may occur in spite of these precautions. Air embolism is not a cause of anxiety (unless due to gross errors of technique), except in patients with a right to left shunt, in which event a few bubbles of air accidentally introduced into the catheter may pass directly into the aorta and cerebral vessels, resulting in a hemiplegia. A similar disaster may, of course, result from the dislodgement of a fragment of thrombus from the catheter tip. A rigor occasionally occurs as a result of foreign protein in the catheter, which, although usually of no consequence, may precipitate cardiac failure in patients with tight mitral stenosis. Thorough cleansing of catheters will avoid this complication.

Zimdahl (1951) has recently reviewed the literature regarding catheter complications: in a total of 1,500 catheterizations collected from various centres, there were 32 complications. In all, 11 deaths have so far been published, and the major risks seem to occur in going beyond the auricle, particularly in patients with ischæmic heart disease, who in any event are liable to ectopic rhythms and sudden death.

The dangers of accidental catheterization of the coronary sinus have been stressed by McMichael and Mounsey (1951), who reported 5 cases in which præcordial pain, collapse, and electrocardiographic changes suggesting myocardial infarction occurred. All cases recovered, but the authors suggest that obstruction of a coronary vein by the catheter may have caused damage to the muscle drained by this vein, with resultant symptoms and signs of cardiac infarction. In one case there was evidence suggesting perforation of the coronary sinus. Catheterization of the sinus can usually be avoided with experience, but still remains a hazard, particularly in persons with coronary artery disease.

CONCLUSIONS

Cardiac catheterization is a valuable and fully justifiable method of investigation in patients in whom accurate data on cardiac function are essential for diagnosis, and for medical or surgical treatment. If carried out by a trained team experienced in the method and in the selection of cases, the risk is extremely small. Nevertheless, a risk remains, and the welfare and safety of the patient should never be forgotten in the search for knowledge.

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HEART DISEASE IN PREGNANCY

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PREGNANCY is a comparatively safe experience for the majority of patients with heart disease: between 1942 and 1947, 500 such patients passed through 596 pregnancies under our supervision with a total of 25 deaths, of which 10 were certainly unconnected with the pregnancy (table 1). In this series the mortality due to the association of pregnancy with heart disease is therefore not more than 2.5 per cent. Nor, in the majority of cases, does pregnancy seem to lead to any deterioration in the cardiac condition, for of the 475 patients who survived, 427 were as well after pregnancy as they had been before. These are cases carefully followed postpartum, and they represent over 90 per cent. of all such cases seen during this period. If it is borne in mind that some of these patients had very severe heart disease and first presented themselves when already in heart failure with the pregnancy far advanced, whilst others insisted on continuing their pregnancy although termination was advised, the risk must be regarded as small in properly selected cases under careful supervision. In addition, the risk must be weighed against the profit, for these 596 pregnancies gave 469 living children, so that approximately 4 out of 5 pregnancies were successful in this respect.

Nevertheless, it must not be forgotten that in a minority of patients with severe heart disease pregnancy is both dangerous and unprofitable. Of 53 such patients in this series, over one-third died and only one in four had a living child. The recognition of these cases is of great importance. When a physician is asked to advise about pregnancy in patients with heart disease he has two duties; first, he must assess the severity of the heart disease and the risk of pregnancy, and next, if he decides that the risk is not prohibitive, he should undertake the task of supervising the pregnancy so that the risk is reduced to a minimum. In this article it is my purpose to discuss the principles upon which assessment should be based and the way in which supervision can minimize the risk. To do this it is necessary first to describe briefly the physiological changes in the circulation during pregnancy, for they determine our attitude to both these problems.

PHYSIOLOGICAL CHANGES IN THE CIRCULATION DURING PREGNANCY

In figure 1 the circulatory changes of pregnancy are represented diagrammatically. The heart output rises progressively until about the 32nd week, and then falls. There is a parallel increase and decrease in the blood volume and in the tissue fluid volume, due to retention of salt and water, possibly owing to endocrine changes. Both these changes are important, for a rise

in the heart output of perhaps 50 per cent. increases the work of the heart, and a comparable increase in the blood volume leads to a liability to failure in the same way as an excessive intake of salt and water.

Even more important than the nature of the changes is the fact that they

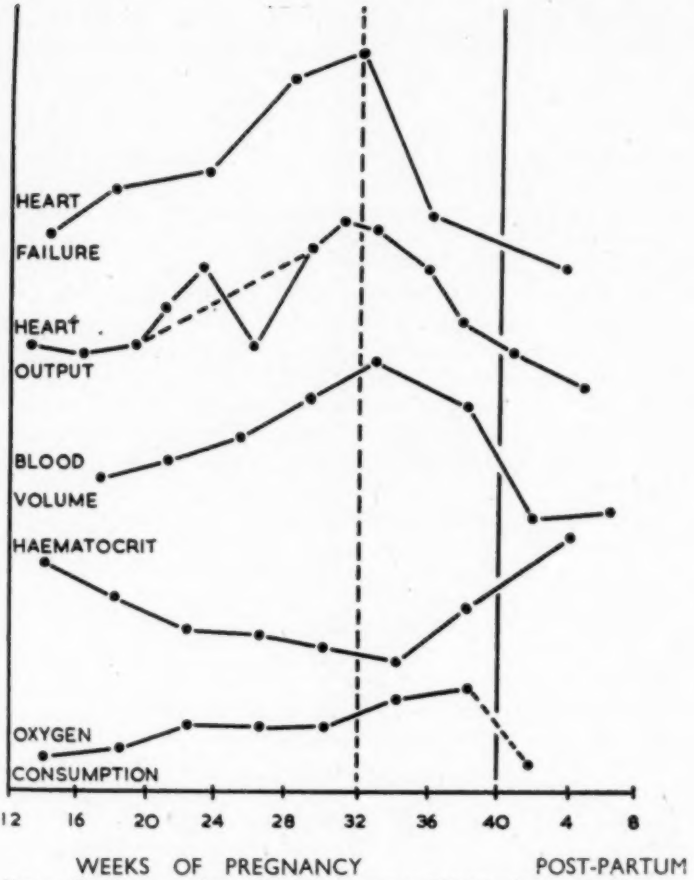

FIG. 1—To illustrate relation of cardiac output and blood volume to incidence of heart failure. The curves are taken from the work of the following authors: heart failure—Hamilton and Thomson (1942); heart output and oxygen consumption—Burwell (1938); blood volume—Thomson, Hirscheimer, Gibson and Evans (1938); hæmatocrit reading—Cohen and Thomson (1936). Reproduced by kind permission of Messrs. Harvey and Blythe Ltd., from 'Heart Disease in Pregnancy'.

reach a maximum well before term and then decline, so that heart failure develops with increasing frequency up to the 32nd week, and then the burden is eased and improvement often occurs (fig. 1). In the past it was

TABLE 1

CAUSES OF DEATH IN 596 PREGNANCIES	
A. Non-cardiac deaths (all postpartum) (3)	
Strangulated hernia	1†
Pneumonia	1†
Miliary tuberculosis	1†
B. Deaths from pulmonary embolism (4)	
Following termination of pregnancy	1
Following spontaneous abortion	1
Following Cæsarean section	1
Following postpartum hysterectomy	1
C. Deaths from heart failure (18)	
During pregnancy	3
Within 8 weeks postpartum	9*
8 months to 4 years postpartum	6†

*In these cases heart failure first appeared during pregnancy.
†In these cases death was not directly attributable to the pregnancy.

often thought desirable to shorten pregnancy by the induction of premature labour or by Cæsarean section, but it is now realized that there is no advantage in this, for the patient's condition is likely to improve and not to deteriorate in late pregnancy. So the high mortality which followed these hazardous procedures has been eliminated.

THE CAUSES OF MATERNAL DEATH

The causes of death in our 25 fatal cases are summarized in table 1. The non-cardiac deaths do not concern us here, and deaths from pulmonary embolism will be reduced principally by trying to avoid interference with the pregnancy by termination or by Cæsarean section. Our main concern, however, is to reduce so far as possible deaths from heart failure, which is the principal danger of pregnancy in these cases.

TABLE 2

FATAL RHEUMATIC HEART FAILURE				
Time of Death	Number of Cases	Number with Acute Pulmonary Œdema	Number with Right Heart Failure	Number with Auricular Fibrillation
During pregnancy or within 8 weeks postpartum	10*	7	3	0
8 months to 4 years postpartum	6	0	6	4

*Excludes one death in very early pregnancy (10 weeks).

HEART FAILURE IN PREGNANCY

Of pregnant women with organic heart disease, 90 per cent. have rheumatic lesions, and the present account is therefore confined to heart failure in rheumatic heart disease. In table 2 the type of heart failure in patients dying during pregnancy or within eight weeks postpartum is compared with the type of failure that occurred more than eight months postpartum. These observations illustrate that the majority of patients who die owing to rheumatic heart failure associated with pregnancy do so because they develop acute pulmonary œdema, whereas in rheumatic heart disease apart from pregnancy, acute pulmonary œdema is uncommon and death is due to right heart failure with peripheral œdema, tender engorgement of the liver, and congested neck veins. *The principal danger of pregnancy in rheumatic heart disease is the liability to acute pulmonary œdema.* There seems no doubt that the reason for this complication is the tendency to œdema associated with the generalized retention of water and salt which is so pronounced a feature of pregnancy. The pulmonary venous pressure is raised by the obstruction at the mitral valve, so tending to localize the œdema in the lungs.

It cannot be too strongly emphasized that the early signs of failure during pregnancy are not found by examination of the neck veins or ankles, but by searching for evidence of increasing pulmonary congestion. It is also wise to bear in mind that right heart failure usually develops gradually and responds well to treatment during pregnancy, whereas acute pulmonary œdema comes on with much less warning and carries a much higher mortality. In this series of cases, 33 patients developed right heart failure during pregnancy, but only 4 died, whereas of 16 patients who had attacks of acute pulmonary œdema, 7 died.

ASSESSMENT OF FITNESS FOR PREGNANCY

Fitness for pregnancy depends principally upon the patient's capacity for effort, for in rheumatic heart disease the degree of exertional dyspnœa is the best measure of the amount of pulmonary congestion. Unfortunately, capacity for effort varies considerably during the course of pregnancy, and assessment must therefore be based principally upon the capacity for effort before the pregnancy, otherwise we cannot compare patients at different stages of pregnancy. If the cardiac condition has been progressively deteriorating before pregnancy, the prognosis is naturally less favourable, and pregnancy should not be encouraged in these circumstances. The best possible indication that pregnancy is not dangerous is a previous trouble-free pregnancy, provided there has been no subsequent deterioration. The most unsuitable cases are those in which there is such a severe degree of pulmonary congestion that dyspnœa occurs on little effort before pregnancy, and especially when there is recurrent hæmoptysis or paroxysmal dyspnœa. Also unsuitable, though perhaps less dangerous, are patients who have had right heart failure during, or apart from, a previous pregnancy.

In general, the history and symptoms are a better guide to fitness for pregnancy than the physical findings, although these are very valuable as a check on the reliability of the history, for some patients exaggerate their disability and others, in their desire to have children, may minimize their symptoms to a surprising extent. The amount of pulmonary congestion shown by radiology is of the greatest importance, for it is the best objective measure of the risk. The presence of auricular fibrillation is usually an indication of a severe degree of rheumatic heart disease, and consequently it has been regarded as a contraindication to pregnancy. In our experience, however, it is not so grave a feature as severe pulmonary congestion or past

TABLE 3

CLINICAL ASSESSMENT OF FITNESS FOR PREGNANCY IN RHEUMATIC HEART DISEASE

Group	Clinical Criteria
I	(1) No dyspnœa during ordinary activity before pregnancy and (2) only minimum radiological cardiac enlargement
II	(1) Moderate dyspnœa during ordinary activity before pregnancy or (2) Moderate radiological cardiac enlargement or (3) Definite but not severe radiological pulmonary congestion but (4) No right heart failure or paroxysmal dyspnœa at any time
III	(1) Severe dyspnœa during ordinary activity before pregnancy or (2) Paroxysmal dyspnœa, recurrent hæmoptysis, or severe radiological pulmonary congestion or (3) Present or past right heart failure or (4) Auricular fibrillation with cardiac enlargement and dyspnœa

heart failure. The size of the heart is of some importance, although many patients with large hearts, but a satisfactory capacity for effort, do well, and moderate cardiac enlargement is not in itself a bar to pregnancy if conditions are otherwise favourable. On the other hand, a small heart may be associated with pulmonary congestion of dangerous severity. The age of the patient is of some importance, for the older patients tend to have more severe rheumatic lesions, and there is evidence that they are also more liable to obstetrical complications. The number of valvular lesions is not of much significance.

It is convenient to have some way of classifying these cases which serves as a general guide to management, and the grouping we have used is given in table 3. Such a classification is to be regarded as a general guide only, for each case must be assessed individually. In group I there is little difficulty, for pregnancy is safe and usually successful (table 4), whereas in group III, pregnancy is always hazardous and usually unprofitable. In group II, however, there is an appreciable risk of heart failure (table 4)

which varies widely from case to case, and each patient must be regarded as an individual problem, taking into account the home conditions, the amount of rest possible, the value of the child (which depends upon the number of living children), the facilities for adequate cardiac supervision during pregnancy, and the capacity and willingness of the patient to cooperate.

THE MANAGEMENT OF TERMINATION

Termination of pregnancy always implies some risk and this increases considerably after the end of the third month, so termination in the second

TABLE 4

PROGNOSIS OF HEART DISEASE IN 596 PREGNANCIES

Group	Number of Pregnancies	Proportion of Living Children	Incidence of Heart Failure during Pregnancy	Mortality from Heart Failure due to Pregnancy
I	200	89 per cent.	0.5* per cent.	Nil
II	343	82 per cent.	7 per cent.	1.1 per cent.
III	53	26 per cent.	47 per cent.	13 per cent.

*1 case of heart failure due to toxæmia with hypertension.

trimester should be avoided if at all possible. There is no advantage in termination during the third trimester. During the first trimester therapeutic abortion will be advised in about 10 per cent. of patients in group II, and in all patients in group III (although only half of these patients seek advice soon enough to make termination practicable). In a few severe cases first seen in the second trimester the increased risk of termination may still be less than the risk of continuing pregnancy. In these cases, and in most cases in group III, therapeutic abortion is a hazardous procedure because the cardiac condition is always poor and sometimes desperate. In such cases termination of pregnancy may seem an urgent necessity, but it must be remembered that the operation of emptying the uterus will make the cardiac condition temporarily worse, not better. On the other hand, adequate treatment of the heart failure will nearly always lead to such rapid improvement that intervention becomes a reasonable surgical risk. *There should NEVER be any question of terminating pregnancy until the cardiac condition has been adequately treated.*

ANTENATAL SUPERVISION

The essence of the management of heart disease during pregnancy is the prevention, early diagnosis and prompt treatment of heart failure. Although the increasing cardiac burden of pregnancy may itself precipitate failure, there are often important additional causes, such as an acute respiratory infection, the onset of anæmia, the development of auricular fibrillation or,

rarely, the onset of bacterial endocarditis. Anæmia is often missed and is a serious and common complication of heart disease in pregnancy. These factors must be promptly recognized and treated if serious failure is to be avoided. Too often deterioration from one of these causes is regarded as an indication to terminate pregnancy, perhaps with disastrous results, when prompt treatment of the cause and of the heart failure would permit the pregnancy to continue safely. In patients with heart disease sufficiently severe to carry some liability to failure, adequate rest is essential to compensate for the increasing cardiac burden of pregnancy; at least ten hours in bed at night and a rest of two hours in the afternoon should be recommended and every effort made to obtain additional help in the home. In such cases acute respiratory infections often precipitate failure, and it is our practice to warn these patients of the importance of treating minor infections seriously by retiring to bed until they are well again.

Early recognition of heart failure.—The importance of increasing pulmonary congestion has already been emphasized. Increasing breathlessness, perhaps a little hæmoptysis, and the appearance of a few persistent moist sounds at the lung bases are ominous signs, and should lead to the institution of proper bed treatment for early cardiac failure. Earlier stages of pulmonary congestion can be recognized if facilities for regular radioscopy of the chest and for the determination of the vital capacity are available, and these facilities should always be available in an organized cardiac pregnancy clinic. Œdema of the ankles is quite common in late pregnancy, and is not an indication of right heart failure unless there is also cervical venous congestion or an enlarged, tender liver.

The treatment of early heart failure.—In pregnancy, treatment should always be undertaken in hospital and follows the usual lines, including salt and fluid restriction and the administration of digitalis, with mercurial diuretics if necessary. In right heart failure the response to treatment is usually good, but it is rarely advisable to allow the patient to return home before delivery, and digitalis should be continued into the puerperium. Acute pulmonary œdema is a much graver condition and should be treated on the spot by morphine, venesection, and oxygen, which may give dramatic relief. Unfortunately, there is a considerable liability to a recurrence which is often fatal, so admission to hospital after recovery from the initial attack is essential, and a full regime for the treatment of heart failure should be instituted.

If heart failure first occurs at about the time of the maximum cardiac burden, the prognosis is good, but the earlier the onset in pregnancy, the graver the prognosis, and heart failure in the first trimester is an indication for therapeutic abortion after adequate treatment of the cardiac condition.

THE MANAGEMENT OF CONFINEMENT

Although the management of confinement is mainly an obstetrical matter, the help of the physician will often be sought when there is anxiety about

the cardiac condition. A normal confinement is well tolerated by patients with heart disease, provided heart failure is not present and dyspnœa has not been severe at the time of the maximum cardiac burden. In the more severe cases it was at one time the fashion to shorten pregnancy by inducing premature labour in the belief that the longer the pregnancy continued the greater the cardiac burden. This technique was soon recognized as more hazardous than a normal confinement and, in an attempt to reduce the mortality, Cæsarean section before term was widely practised, especially in the United States. Now that it is realized that the cardiac burden diminishes in the later stages of pregnancy, there is no indication to shorten gestation, and we have been encouraged to allow these patients to have a normal confinement at term, even when heart failure has occurred. There is now fairly general agreement that this reduces the mortality; for instance, in 26 patients with severe heart disease delivered by Cæsarean section, Mendelson recorded 3 deaths, whereas of 136 patients (selected because their heart disease was of comparable severity) delivered vaginally, none died. In the present series of 596 pregnancies only 10 Cæsarean sections were undertaken for cardiac reasons, all in the first 300 cases. We now consider that there is almost no cardiac indication for Cæsarean section, with the possible exception of coarctation of the aorta, in which rupture of the ascending aorta may occur owing to the physical strain of labour.

If the obstetrical situation is not satisfactory, however, and there is the likelihood of a difficult labour, Cæsarean section will be considered more readily in a patient with severe heart disease than in a normal woman, for at all costs a difficult forceps delivery must be avoided in an exhausted patient whose cardiac condition is rapidly deteriorating. Most obstetricians consider that there is no place for trial labour in the management of these cases.

The dangers of the confinement have been exaggerated in the past, and we now believe that the danger of heart failure is greater during the period of maximum cardiac burden than during a normal labour. Provided the confinement is skilfully conducted, the mode of delivery is less important than the cardiac condition of the patient at term, and that depends largely upon adequate supervision during pregnancy.

CONCLUSION

The precepts we follow can be summarized quite briefly. As often as possible allow pregnancy to pursue its normal course, but beware of pulmonary congestion and guard against heart failure with constant vigilance, especially watching for complications such as anæmia and searching for signs of increasing pulmonary congestion. If failure appears, treat it promptly and thoroughly. Eschew all modes of interference with the confinement, unless there are obstetrical difficulties; and finally, if any interference with the pregnancy becomes essential, never permit it without first making every attempt to improve the cardiac condition.

NICOTINAMIDE AND PELLAGRA

A REVIEW OF THE DEVELOPMENT OF KNOWLEDGE AND OF THE PRESENT POSITION*

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In the growth of knowledge about pellagra during the last forty years, contributions from Britain, the United States, Germany and elsewhere have all played a part. The theory that pellagra was a vitamin-deficiency disease was first put forward by Funk, working in London in 1912; and the first conclusive proof that pellagra could in fact be controlled by the diet and was not due, for example, to an infection, was furnished in 1914-15 by Goldberger in the United States.

In 1920, Voegtlin, also in the United States, proved the existence of a pellagra-preventing factor, which occurred in association with crude 'vitamin-B extracts', but was distinct from the anti-beriberi principle; and in 1926, Goldberger differentiated the pellagra-preventing factor from the anti-beriberi vitamin, by its greater heat stability, and by differences in its distribution and solubility. In 1935, the P-P factor was further differentiated by Birch, György and Harris at Cambridge as a component of the vitamin B complex, distinct not only from vitamin B_1, but also from two additional 'B' vitamins, viz. vitamin B_6, and riboflavin.

Elucidation of the nature of the P-P factor has been facilitated by the production of analogous experimental deficiency diseases in dogs (Goldberger, 1926), in monkeys (Harris, 1937, 1938), and in pigs (Birch, Chick and Martin, 1937, 1938)—both the latter groups working at Cambridge. Experimental diseases which were formerly regarded as the true analogues of pellagra, such as 'rat pellagra' and 'chicken pellagra', were subsequently shown to be due to deficiencies of other vitamins (vitamin B_6 and pantothenic acid, respectively).

To turn to the history of nicotinamide†, now recognized as the true P-P vitamin. This substance was first detected as occurring in association with 'vitamin B' extracts by Funk, in 1913-14, and by Suzuki in Japan; much later, in 1935, it was identified as a component of certain co-enzyme systems

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†I.e., nicotinamide or nicotinic acid, since the latter can be regarded as sharing the biological activity of the amide, being converted to it in the body.

by Euler *et al.* in Scandinavia, and by Warburg and Christian in Germany. It was next shown in 1937 to be a dietary essential for various micro-organisms, both by Knight in London, and by Mueller in the United States; and, finally—also in 1937—it was found to cure experimental pellagra in dogs (Elvehjem *et al.*, in the United States). Before long it had been demonstrated to be equally effective for monkeys (Harris), for pigs (Chick *et al.*), and for the cure of pellagra itself in man (Fouts *et al.;* Spies *et al.;* Harris and Hassan).

THE CLINICAL PICTURE OF PELLAGRA

As seen clinically, pellagra is not uncommonly a multiple deficiency disease, complicated by the presence of such additional symptoms as polyneuritis and cheilosis (attributable respectively to lack of vitamin B_1 and of riboflavin). Nevertheless, the basic symptoms which should be regarded as specifically pellagrous are those due to lack of the anti-pellagra vitamin itself and are cured by its administration, namely—(1) the highly characteristic skin lesions: (2) glossitis and stomatitis, including the 'beefy tongue'; (3) persistent diarrhœa; and (4) mental symptoms.

Outside regions of endemicity of pellagra, e.g., among depressed populations in maize-eating areas, so-called *secondary pellagra* (conditioned deficiency of nicotinamide) may be found in association with conditions causing inadequate ingestion, absorption, or assimilation of the vitamin, as for example with chronic alcoholism, with gastro-intestinal obstruction; and also among mental patients.

The nutritional status of a patient in nicotinamide may be assessed by determination of the excretion of nicotinic derivatives after loading doses, as suggested in 1937 by Harris and Raymond.

NICOTINAMIDE THERAPY IN PELLAGRA

In the treatment of pellagra, doses of 500 mg. nicotinamide per day have been given at first, and reduced later to 50 to 100 mg. per day or less; dramatic improvements in the mental condition are recorded within a few hours, and of the lesions of the skin and mouth within a few days. At the same time, stress is laid on the importance of correcting any other concurrent deficiencies.

Experiments on nicotinamide deficiency in rats, e.g., by Krehl and his colleagues in the United States, and by Harris and Kodicek and others in this country, have indicated the existence of other pellagragenic factors in addition to a simple deficiency of nicotinamide—such are (1) a deficiency of protein, particularly of its constituent amino-acid, tryptophan (and possibly an imbalance of amino-acids); (2) the presence in the diet of maize (possibly containing some positive pellagragenic agent); and (3) perhaps a lack of (or a variable degree of) micro-synthesis within the alimentary canal—as suggested by the work in London of Ellinger and Benesch, 1945.

TRYPTOPHAN AND PELLAGRA

We now know from the work of American teams, that tryptophan is converted to nicotinamide in the animal body, and hence it acts as the precursor of the P-P vitamin. Thus, two older rival views are now reconciled: that pellagra was due (a) to absence of a vitamin, or (b) to poor-quality protein, deficient in tryptophan. And at this point we must recall that the pioneer worker in the isolation of tryptophan, and in demonstrating its influence on the biological value of proteins, was Sir Frederick Gowland Hopkins, O.M., for many years Professor of Biochemistry at Cambridge. Another pioneer was the Englishman, Professor W. H. Wilson, whose studies in Egypt in 1921 had stressed the importance of poor quality protein in the causation of pellagra.

ESTIMATION OF NICOTINAMIDE

Nicotinamide has been estimated by (1) biological tests; (2) microbiologically (as in the method developed in America by Snell and Wright, 1941); and (3) by chemical colour reactions, e.g., the methods worked out in India by Swaminathan in 1938, or in Cambridge by Harris and Raymond, 1939. It must be recognized that the biological test measures the over-all 'anti-pellagra' activity (*vide supra*), and not merely the nicotinamide content.

PHYSIOLOGICAL ACTION

As to its physiological rôle, nicotinamide is known to be a component of the two essential 'pyridine co-enzymes', i.e., the pyridine nucleotides: (1) co-dehydrogenase I, or di-phosphopyridine nucleotide, and (2) co-dehydrogenase II, or tri-phosphopyridine nucleotide. These are present in all animal tissues and are concerned in hydrogen transfer in the living cell. Nevertheless, the chemical lesion in pellagra is still somewhat obscure, and it is by no means certain that the error lies simply in the defective activity of these co-enzyme systems.

CONCLUSION

As distinct from replacement therapy, i.e., in the cure of deficiency disease, the administration of nicotinamide, pharmacologically, has been said to help animals exposed to anoxia, or human beings in the performance of agility tests; it is not yet clear whether these observations may have practical applications in medicine or dietetics.

SOCIAL AND MEDICAL ASPECTS OF TATTOOING

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'Ye shall not make any cuttings in your flesh for the dead, nor paint any marks upon you.'—*Leviticus*, xix, 28.

ALTHOUGH the practice of tattooing is probably less widespread in this country at the present time than it was half a century ago, its popularity certainly increased in the armed Forces during the recent war, and the medical aspects of this curious custom have more than a theoretical interest.

GEOGRAPHICAL DISTRIBUTION

To the social anthropologist there is no fundamental distinction between tattooing by puncture and other techniques of body marking. There is no geographical limit to the practice of painting or scarification, the distribution of which was world-wide, and tattooing has tended gradually to replace these other forms of body marking except in those races with very dark skins, such as the Australian aborigines, the Bantu and the Melanesians, among whom scarification has persisted. The ritual and magical associations of painting and scarification have been transferred to tattooing, which has the advantage of combining permanence and wider scope for the elaboration of complex designs (Buckland, 1887-88).

HISTORY AND ORIGINS

Although painting and scarification were widely distributed in prehistoric times, the earliest known puncture tattooing was in Egypt, certainly 2000 B.C. and possibly 4000 B.C. The practice was associated with fertility rites, ideas of heaven, and with social status. It was perhaps derived from the Egyptians by the Polynesians, and Polynesian incursions probably introduced the custom to the American Indians.

Moses (*Leviticus*, xix, 28) forbade tattooing as idolatry and it was condemned by Mohammed in the Koran. However, it is said to be widely practised by certain Arab tribes, who tattoo a small blue cross on the glabella or cheek of young girls, removing the mark with quicklime and soap at the time of marriage. These tribes are said to justify their departure from the teaching of the Koran by their claim that purification by fire before entering Paradise will remove their tattoos together with other earthly impurities.

Herodotus mentions that in Thrace women of noble birth were tattooed. Tattooing by puncture was practised in Europe before the Christian era, and its popularity with the early Christians in Britain was such that it was prohibited in certain religious orders at a council in Northumberland in A.D. 787.

There is, however, little information available on the history of tattooing in Western Europe in historic times until the eighteenth century. It is certain that seamen, travellers and pilgrims were occasionally tattooed, but there is no reliable evidence as to the extent to which the art was practised at home. The word tattoo was introduced to Europe from Polynesia by Captain Cook, who originally spelt it 'tattow' (the native pronunciation is said to be Tatahou). There is, however, no reason to believe that Cook's men were responsible for introducing or reintroducing the art to Europe.

Parry (1933) gives a popular account of puncture tattooing in the contemporary United States. He describes the fluctuations of popularity which the practice has undergone in the past century, and the surprising extent of tattooing in men and women in high society in Britain as well as the United States in the later years of the nineteenth century.

MOTIVES

For a detailed account of the significance of tattooing in various primitive peoples, and the rites and ceremonies with which it is associated, the monograph by Hambly (1925) should be consulted. The tattoo has been employed for simple identification during life or for identification in heaven, either by the Deity or, as among the Nagas, by husband or wife. It has been widely used to ward off evil spirits, as part of the marriage ceremony or in the cure of sickness. It may be a totemic device identifying an individual with his group, or a mark of social status. Among some peoples the tattoo is used to record prowess in the hunting field or in battle. Certain tribes of head hunters record their homicides with stars and other emblems. Sometimes the ordeal of tattoo is a recognized test of courage, as among the Thompson Indians of British Columbia (Teit, 1927-28). By far the most frequent practice, however, associates tattooing with the rites of puberty, marriage and fertility, and an intimate connexion between body marking and puberty and marriage rites is found in North and South America, India and the Pacific area.

The motives which induce contemporary man to be tattooed are no doubt somewhat different from those influencing primitive man, but it may well be that, as is the case with so many ancient customs which have persisted to modern times, the original motives have survived under the cloak of acceptable rationalizations. Lombroso in Italy in the last century was impressed by the number of criminals who were tattooed, and he came to regard the tattoo as an atavistic trait.

Bromberg (1935), a psychiatrist, considers that tattooing is related to emotional immaturity. He states 'contrary to Lombroso's opinion, tattooing seems more a manifestation of a neurotic conflict depicted on the body surface than an atavistic regression to a primitive love of adornment'. He claims that two types of men have tattoos, the clearly exhibitionist type, often a sailor, who adds to his collection over the years, and the younger man who bolsters his feeling of inferiority by identification with strong men. He chooses designs of stalwart warriors, snakes or lions. Latent homosexual factors may determine the choice of designs proclaiming heterosexuality, and sadistic elements may lead him to choose designs incorporating skulls, daggers or spears.

We have recently seen a young man who is sexually impotent and who has numerous war-like designs on both forearms. Other cases in our recent experience also lend support to Bromberg's views. Nevertheless, we have seen many apparently stable individuals who have been tattooed during an evening of alcoholic celebration early in their Service careers. Bromberg (1935) states that the decision to have a tattoo is made impetuously, often in an alcoholic state as considerable resistance has to be overcome, owing to a natural unwillingness to deface the narcissistic organ.

Simons (1948) gives an interesting account of an epidemic of tattooing among British prisoners in a Japanese prisoner of war camp in Java. The craze began about three months after capture and persisted for a period of six months, during which time a large number of the prisoners under twenty-two years of age were tattooed. After six months the craze quite suddenly came to an end.

The motive here must presumably have been a desire for identification with the herd. Tattoos were often inflicted for the basest of motives in the concentration camps in Germany in the recent war.

TECHNIQUES AND DESIGNS

Puncture tattoo involves the introduction into the dermis of particles of insoluble pigment. Of the variety of techniques employed by primitive peoples the most simple consists in outlining the design in soot or charcoal and driving the particles into the skin with a thorn. The modern artist employs an elaboration of this technique, and uses a special electric needle or a battery of needles. The pigments most commonly employed are carbon (in the form of Indian or Chinese ink) for the blue-black colour, cinnabar (red), ochre (brown), chromic oxide or hydrated chromium sesquioxide (green) (Rostenberg *et al.*, 1950).

The actual operation may be painful but in the hands of a skilful artist is rapidly completed. An inflammatory reaction develops and persists for from ten days to three weeks, being usually more severe with the metallic pigments. The modern artist is aware of the necessity for antisepsis, but the practice of mixing the pigments with saliva or of holding the needles in the mouth used to be common, and many artists apply saliva to the design to relieve the initial pain.

The pigment particles lie in the cutis or subcutis, chiefly around the blood vessels, and are largely extracellular, but some may lie intracellularly, and in this site may possibly dissociate and form organic substances capable of acting as haptens. The permanence of the design has been carefully investigated on account of its occasional medico-legal importance. Whereas most designs will persist for life, some, especially those in vermilion (cinnabar), tend to fade and may disappear completely, perhaps on account of the brisker inflammatory reaction provoked by this pigment. Goodman (1946) claims, however, that blue and black designs fade the most rapidly. Pigment particles can often be found in the regional lymph nodes.

Lacassagne (1881) studied 1,333 *designs* in 378 members of a French battalion. He classifies the designs, and illustrates many of them. Religious,

occupational, military, and erotic designs were common. Schonfeld (1930) illustrates many designs which had recently become popular in Germany, and points out that the majority are merely modern versions of familiar basic themes, the cowboy hero, for example, replacing the lion or the dragon. Parry (1933) describes and illustrates large numbers of the designs which are most popular in the United States. Here, again, the limited range of basic themes in the designs is striking. The tattoo artist's client apparently prefers the conventional to the original. The artistic merits of the designs vary widely, the highest perfection being achieved by Japanese artists.

MEDICAL ASPECTS

The medical aspects of tattooing attracted little attention until Berchon (1869), a French naval surgeon, made an exhaustive study of the subject. His work still makes interesting reading and contains much curious information. His main object was to draw attention to the possible risks of tattooing, in the hope of persuading the Naval authorities to forbid the practice.

Pyogenic infections.—In view of the insanitary techniques employed by the earlier artists it is hardly surprising that infection should have occurred from time to time. The dramatic sequelæ to the introduction of pyogenic infection in certain cases were naturally the earliest to attract attention, and in 1820, Lesson recorded a case in which sepsis had necessitated amputation. Rayer mentions erysipelas as a complication. Berchon collected eight cases of local gangrene, and he mentions four deaths after amputation and three other deaths directly resulting from tattooing. We have found no such case in the recent literature.

Syphilis.—The possibility of transmitting syphilitic infection in the act of tattooing was realized by Hutin as long ago as 1853.

Maury and Dulles (1878) examined 22 clients of an artist with secondary syphilis with mucous patches. Fifteen of the 22 had acquired syphilis by tattooing. Whitehead (1889) found primary lesions in the tattoos of 5 of 12 men tattooed by a man with mucuous patches, and Barker (1889) reported 12 cases contracted from a hawker tattooist. Hamada in Japan found a positive Wassermann reaction in 20 per cent. of 265 tattooed iron-workers, and suggested that tattooing was responsible for the transmission of a significant number of cases of syphilis. Rukstinat (1941) of Chicago reported on 9,510 post-mortem examinations: 8.79 per cent. of white male adults and 0.71 per cent. of females were tattooed. The evidence of syphilitic infection was not significantly higher among the tattooed, and Rukstinat concluded that the disease is not transmitted by tattooing to any appreciable extent in the United States.

Tuberculosis.—Occasional instances of the inoculation of tuberculosis by tattooing have been recorded. Collings and Murray (1895) recorded the case of a boy of fifteen with pulmonary tuberculosis who tattooed his two brothers and a friend, all three of whom developed primary tuberculous lesions in the tattoos, and Heller observed tuberculosis in a tattoo rubbed with tuberculous milk.

Leprosy.—Whether or not leprosy can be transmitted by inoculation is

doubtful, as workers who have endeavoured to inoculate themselves or volunteers have failed to do so. However, two members of the United States Marine Corps who were tattooed by the same man on the same day in Melbourne in 1943 developed maculo-anæsthetic tuberculoid leprosy in their tattoos in the first half of 1946 (Porritt and Olsen, 1947). Circumstantial evidence suggests that the infection was transmitted by inoculation, but it is possible that it was acquired in some other way, and that the lesions were merely first manifest at a site of low-grade inflammation.

Vaccinia has developed in a tattoo which had been performed three weeks before vaccination near the upper border of the design (Wilde, 1929).

LOCALIZATION OF SKIN DISEASE IN TATTOO

Syphilis.—When the eruption of either the secondary or the tertiary stage of syphilis develops in a tattooed individual it may show a predilection for the tattooed area in which it may either first appear or be accentuated.

For example, Dohi (1926) reported a case in which heavy clusters of papules appeared in the blue areas of the tattoo of a man aged thirty-five who had been tattooed at the age of nineteen. Dohi was the first to observe that the red areas were spared. Holland (1911) saw three patients in whom a tertiary syphilide was localized in a blue tattoo, and another patient in whom the red areas of the tattoo were involved more heavily than the blue. In the latter case the red pigment was probably carmine. Florange (1909) observed a syphilide which involved the blue areas of the tattoo but spared the red areas, and this is by far the more usual happening, as cinnabar is a mercurial compound. Belote (1928) reviewed the literature on this subject and supported the claim that cinnabar suppresses the eruption. He cites some early experimental work and reports two further cases.

Psoriasis and lichen planus.—Psoriasis can develop in a tattoo but shows no predilection for any colour. The tendency for psoriasis to develop at any point of trauma or chronic inflammation is well known (Koëbner phenomenon). Lichen planus, which similarly shows the Koëbner isomorphic phenomena, has also been recorded in tattoos.

Foreign body reactions.—When the wide diversity of materials which may be introduced is considered, the rarity of foreign body granulomas in tattoos is surprising. Madden (1939) reported the case of a man aged twenty-seven who developed dark-red nodules in a tattoo which had been present for seven years. The histology showed a sarcoid type reaction. This patient may be compared with that of Sweet (1950) who developed sarcoid lesions at sites of accidental introduction of foreign particles. The unique case of Auger (1943) concerns a man aged thirty-three, tattooed seventeen years before with the blue design, who developed in the tattoo a firm tumour which on histological examination proved to be a reticulosarcoma containing pigment.

Allergic reaction to the pigments.—The most frequent and by far the most important reaction observed in tattoos depends upon the development of an allergic hypersensitivity to cinnabar or to an organic mercurial compound derived intracellularly from cinnabar. In a typical case the patient tattooed months or years previously complains of severe irritation and swelling con-

fined to the red areas of the design. In Madden's (1939) patient the red areas had remained raised, crusted and pruritic since the tattoo was performed, the initial reaction having failed to subside. Usually, however, there is a latent period before symptoms develop. In most cases the sensitivity to cinnabar develops spontaneously, but sometimes the application of a mercurial preparation to another skin area has apparently induced the sensitivity to mercury which has then become manifest in the red areas of the tattoo. Patch tests give conflicting results. Madden found them positive to 2 per cent. ammoniated mercury, mercury ointment and 1 in 100 mercury perchloride, but negative to cinnabar. Sulzberger (1937) found the tests positive to ammoniated mercury, mercury perchloride and cinnabar. Duncan and Johnson (1947) found them negative to cinnabar but positive to ammoniated mercury. The inconsistency of these findings lends weight to the suggestion that hypersensitivity may develop primarily not to cinnabar itself but to a derivative compound. The reaction in the tattoo may persist indefinitely and the patient may request excision of the affected area for relief of the pruritus, which may be severe. There may, however, be spontaneous diminution of sensitivity with subsidence of the reaction, as in the patient of Sulzberger, Kanof and Baer (1944). On the other hand the reaction may extend beyond the limits of the tattoo, and Swinney's (1946) patient had a widespread exfoliative dermatitis which settled only after excision of the tattoo. The case recorded by Rostenberg *et al.* (1950) is exceptional in that a reaction of a similar type was limited to the green areas.

Lupus erythematosus.—Madden (1949) reported the case of a man aged thirty-six who developed lupus erythematosus simultaneously on his face and in the red areas of his tattoo. Flares of face and arm followed exposure of the face only to sunlight. Rook and Thomas (1951) have observed a similar case. It is doubtful whether the appearance of lupus erythematosus in the tattoo in this patient should be regarded as an isomorphic phenomenon, or whether sensitivity to mercury is a causative factor in the lupus erythematosus. In favour of the latter alternative is the restriction of a reaction to the red areas of the tattoo, and the presence of a strongly positive patch test to ammoniated mercury in the second patient.

REMOVAL OF TATTOOS

A request for the removal of a tattoo is often made, either because the design recalls a past episode which the patient wishes to forget, as when the tattoo has been inflicted in a concentration camp, or when some frivolous or erotic design is causing the patient social embarrassment.

When the patient to whom the difficulties have been explained insists upon the removal of the design, the following procedures can be considered:—

(1) In the case of a small tattoo, good results can be obtained by diathermy coagulation, but in most cases of tattoos of small or moderate size excision with or without grafting is the treatment of choice.

(2) When the design is very large the chemo-surgical technique of Lerner

(1948) can be employed. We have had no personal experience of its use but it would appear to be a painful procedure. The subject is discussed by Lacassagne (1944), who describes other techniques which have been recommended and gives many references to other authorities.

(3) Sometimes the patient is best advised to visit another tattoo artist who can either alter the incriminating initials or clothe the naked figures, and most artists are often called upon to make such changes in existing designs.

SUMMARY

A brief account is given of the origins, history and techniques of puncture tattooing, and the more important medical complications of the procedure are reviewed. A volume would be required to cover the enormous literature on tattooing, and therefore only the most useful references have been selected. Those marked with an asterisk include lengthy bibliographies. Accidental, occupational and therapeutic tattooing have not been considered.

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GENERAL PRACTITIONERS' FORUM

INTRAVENOUS IRON TREATMENT IN GENERAL PRACTICE

By BERNARD ISAACS, M.B., Ch.B., D.R.C.O.G.

In the October 1951 issue of *The Practitioner*, Professor L. S. P. Davidson and Dr. James Innes wrote about the place of intravenous iron therapy in general practice. They concluded:—

'Intravenous iron therapy has undoubtedly proved a valuable advance in hæmatological treatment, but it must be emphasized again that the indications for it are strictly limited, and it should be employed only in selected cases after a thorough trial of oral medication.'

During 1951, I had been treating a small number of patients with iron intravenously, and I should like to record my own conclusions. These are: (1) opportunities for using intravenous iron treatment are fairly frequent in general practice; (2) the principal drawbacks are that time and care are needed and the treatment can produce unpleasant side-effects; (3) the results of treatment are good, and the advantages outweigh the disadvantages.

SELECTION OF CASES

I have used intravenous iron treatment in eleven cases during a year spent in general practice. In selecting these cases for treatment I have adhered to two principles.

(1) *Iron deficiency must be established beyond reasonable doubt as the cause of the condition.*—To give iron in secondary anæmia without determining the cause is much the same as to give morphine in undiagnosed abdominal pain. Of my eleven patients, two were pregnant women who were found to have severe hypochromic anæmia on routine testing; two were postnatal cases who had suffered excessive blood loss during parturition. The remaining seven patients were women whose ages ranged from twenty-eight to fifty, and who had a history of numerous pregnancies or heavy menstrual losses. These patients attended initially complaining of pallor, fatigue and debility of long duration, and in some cases there was a more recent onset of breathlessness on exertion, œdema of the ankles, præcordial discomfort, and calf muscle pains. A general examination in every case showed no evidence of such primary diseases as malignancy or tuberculosis, and no signs of glossitis. The blood examination consisted of a Sahli hæmoglobin estimation and inspection of a stained film. When these showed a low hæmoglobin value, but not below 7 g. per cent., and a hypochromic microcytic picture, I considered a diagnosis of primary iron deficiency to be established beyond reasonable doubt.

The cases selected for treatment thus fall into three categories: (i)

idiopathic iron-deficiency anæmia of women; (ii) iron-deficiency anæmia of pregnancy, and (iii) post-hæmorrhagic anæmia.

(2) *Anæmia which is causing serious ill-health should be treated with vigour until cured.*—Therefore in severe anæmia, intravenous iron is in my opinion the first choice in treatment, just as oral iron is the first choice in mild anæmia. In this I differ from Davidson and Innes, who require a thorough trial of oral iron before resorting to intravenous treatment. My reason is one which I think every general practitioner will appreciate—the difficulty of supervising a patient on oral iron treatment. Without doubt oral iron should completely cure most hypochromic anæmias, but in practice it must often fail to do so. The patient who responds well to treatment seldom persists with it until cure is complete, because she is feeling better; the patient who develops gastro-intestinal disturbances stops taking her iron and does not come back to see the doctor. Four of my seven cases of primary anæmia had

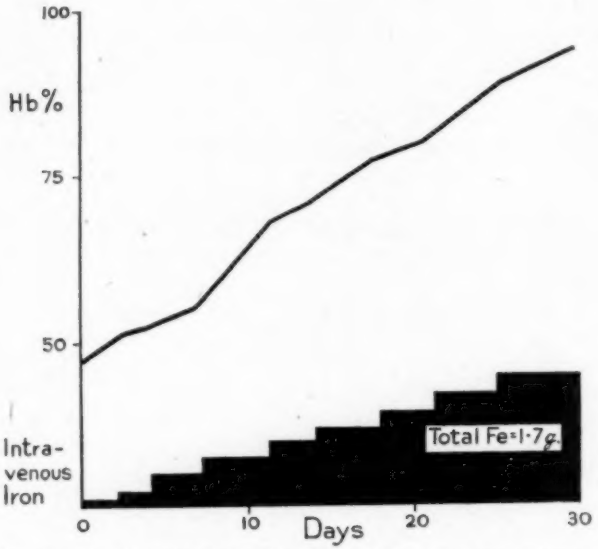

FIG. 1.—Mrs. H., aged forty-six, three children. Still menstruating, periods always very heavy, cycle 7/28. Complained of excessive fatigue, breathlessness, præcordial pains and cramping pains in legs on exertion. The figure illustrates the rise in hæmoglobin on intravenous iron treatment.

previously been treated by other doctors with oral iron, yet when I saw them the hæmoglobin level in each was below 60 per cent.

These arguments do not apply to the injection treatment, for patients on any form of injections rarely default. Should toxic symptoms arise it is at the doctor's discretion to stop or continue the treatment, not at the patient's.

On account of the potential toxicity of iron given intravenously, however, I agree that it should be reserved for the more severe anæmias. I have used it as a first treatment only when the hæmoglobin reading was below the arbitrary figure of 60 per cent. Sahli, equivalent to 8.7 g. per cent.

DOSAGE

The preparation I have used is 'ferrivenin' (Benger). The makers state that a 5 ml. ampoule, containing 100 mg. of elemental iron, should in theory produce a hæmoglobin rise of 4 per cent., but that in practice the rise is usually about $2\frac{1}{2}$ per cent. In my own experience the figure was nearer 3 per cent., and I accordingly calculated the total course required by subtracting the patient's hæmoglobin percentage from 100, and dividing by three to give the number of ampoules to be administered, e.g., a patient with a hæmoglobin of 52 per cent. will require a course of sixteen ampoules (≡1.6 g. of iron). The maximum amount that can be given safely in a single injection is 200 mg., and I found that nothing was gained in safety, and certainly nothing in convenience, by using a smaller dose. I tried giving the injections daily, every second day or twice a week, and found the last method most satisfactory.

Figure 1 illustrates the response in a typical case to what became my standard course, i.e., 50 mg. on the first day, 100 mg. on the third day, 200 mg. on the fifth day, and thereafter 200 mg. twice a week.

PRACTICAL DIFFICULTIES AND TOXIC EFFECTS

An injection of 10 ml. cannot be given properly in less than ten minutes, which is a big fraction of a consulting hour. I therefore arranged for the patients to attend at a special time, or visited them in their own homes.

I encountered three main difficulties in administering the injections—escape of iron solution from the veins, thrombosis, and venous spasm. To these I should perhaps add absence of veins, for a patient not in this series was selected for treatment but never received an injection, as I could find no suitable vein. To minimize escape of the injection into the tissues I used a good screw-type tourniquet and a small (no. 14) serum needle; but even so, this painful accident occurred on several occasions, mainly in the earlier cases. The most unfortunate of these was a very nervous woman who invariably pulled her arm away just as the needle entered the vein, and she thus inevitably received several subcutaneous injections. I managed to give her half the calculated course with good effect, but she became so apprehensive of the injections that they had to be abandoned. To avoid the other two difficulties mentioned I always diluted the iron preparation with the patient's blood before injecting the mixture, very slowly. Severe pain along the course of the brachial vein following the injection, presumably due to spasm of the vein, occurred only once, but I was less fortunate with vein thrombosis, which I met with in four patients. In one of these the only two

suitable forearm veins became thrombosed in turn, and this course also had to be abandoned when only half complete.

Of the toxic effects of the injections the one that gave most trouble was a peculiar pain in the back coming on about five minutes after the injection. This occurred in six of the eleven patients treated, and varied from a slight ache to a severe pain. In four of these the pain was present on two or three occasions only, and lasted for five or ten minutes. I must add that when I expressed concern over this reaction each patient insisted, 'It's all right doctor, it's nothing. Please carry on with the injections'. The fifth patient had the pains four times, early in her course, and then not subsequently. She described it as an unpleasant throbbing sensation, 'like electricity'. The sixth patient had extremely severe back pains five minutes after injections—'like labour pains, only worse'—with flushing, sweating and restlessness, lasting five to fifteen minutes before gradually passing off. She had this six times, as she too did not wish the injections to be stopped. I found that I could prevent the pain by reducing the injections to 50 mg., and on switching to 'iviron' (British Schering) gained the impression that this preparation was less liable to cause pain in this patient than 'ferrivenin' in the same dose. This patient eventually received her full calculated course in 50 mg. injections without further toxic effect and with excellent hæmatological result.

Four patients had general reactions, occurring three to twelve hours after injection, and after only one or two injections in the course. These consisted of shivery feelings, flushings, a sensation of weakness, and a heavy aching pain in one shoulder. An alarming reaction occurred in one patient not included in this series. She was pregnant, within a fortnight of full term, and her hæmoglobin was 68 per cent. I was tempted, against my better judgment, to try to give her hæmoglobin a quick boost. Within a few seconds of receiving her first injection of 50 mg. of iron she felt very weak and dizzy, turned extremely pale and almost fainted. Her pulse remained strong and she recovered completely within a few minutes, but she received no further injections. She had a healthy baby at term.

Six patients had mild gastro-intestinal upsets during the treatment: constipation, diarrhœa, colicky abdominal pains, and in one case vomiting. Two patients said they had had black stools. The treatment was not interrupted because of these symptoms.

RESULTS

The results of the treatment were excellent. Two patients did not complete the course: one because of thrombosis of all available veins, the other because of fear of the injections. A third patient was unable even to start treatment as no suitable vein could be found. In the remaining nine patients treatment resulted in a rapid and satisfactory rise of the hæmoglobin to 100 per cent., the case illustrated in figure 1 being a typical example. Patients who had been anæmic for years suddenly felt extremely well, with a striking

change in their colour, vigour and general appearance, which was immediately remarked on by their friends. It was also a gratifying experience for the doctor, whose work seldom yields such plainly visible results.

My conclusion is therefore that intravenous iron therapy in general practice is laborious, and is almost invariably attended by unpleasant reactions. These do not, however, constitute a real danger to the patient, and the more skill and care the doctor employs, the less trouble he is likely to meet. The satisfying results that can confidently be expected in properly selected cases justify, in my opinion, the use of intravenous iron in general practice as the first treatment of *severe* iron-deficiency anæmia.

AN HYPOTHESIS RELATING TO THE RENAL CIRCULATION IN ACUTE NEPHRITIS

BASED ON A CLINICAL OBSERVATION

By JACK CARR, M.R.C.S., L.R.C.P.

During the treatment of a case of acute nephritis in an adult male it was observed that whilst specimens of urine passed during the day were loaded with albumin, certain night specimens were totally free of albumin. This case of acute nephritis was typical in all respects; it followed shortly after a sore throat and presented all the usual signs and symptoms, including marked œdema and heavy albuminuria. It was while these signs were still evident that the phenomenon of albumin-free urine passed during the night was observed. The patient made a complete recovery, and during the recovery phase an anæmia typical of the disease was noted. From the onset, the signs, and the complete recovery there could be no doubt of the diagnosis of acute glomerulonephritis.

The degree of albuminuria is generally taken as one of the criteria of the severity of this disease, and its disappearance as one of the signs of recovery. Although it has long been recognized that the degree of albuminuria varies during the course of the disease, the observation that the urine may be albumin-free in certain night specimens, while day specimens are still loaded, is an observation which appears to have escaped the notice it merits. Discussion with clinicians has indicated that this phenomenon has been noticed by some and not by others. The observation is significant because an attempt to explain it would throw light on some aspects of kidney disease and, incidentally, on changes in the body associated with sleep. This almost dramatic disappearance of albuminuria could only be brought about by some change in the circulatory or nervous mechanism of the kidney. A sudden change in cell pathology would be difficult to entertain.

The explanation of this phenomenon might be forthcoming from recent studies on the renal circulation. Among these the work of Trueta and his colleagues (1947) in Oxford, and the studies of Platt and his colleagues (Black, *et al.*, 1948) in Manchester, are of note. The shunting of the renal circulation in kidney disturbances as described by Trueta, and the anatomical differences in the glomeruli and circulatory paths in the cortical and medullary regions of the kidney would appear to explain the phenomenon observed. Trueta describes the kidney with two potential circulations—a greater and a lesser. In extreme conditions the blood may pass exclusively through one or other of two pathways. The vessels making up the pathway of the greater circulation are associated with the cortical glomeruli, the channels of the lesser with the glomeruli nearer the medulla—the juxta-medullary glomeruli. The calibre of the efferent vessels of these juxta-medullary glomeruli is far in excess of any other arteriole, afferent or efferent, in any section of the kidney, and the loop of Henle associated with this juxta-medullary vasculo-nephron unit passes deep into the medulla. When a renal shunt is present the route taken by the blood is through the juxta-medullary glomeruli, their efferent vessels and derivative vasa recti to the interlobular veins.

Platt and his colleagues, on the basis of inulin and diodrast clearance observations, postulated the changes in the renal circulation in acute nephritis as a generalized constriction of the afferent vessels to the glomeruli, with a dilatation of their efferent vessels, and a diminished blood flow through the kidney. The inulin clearance, which is a measure of glomerular filtration, was found to be reduced, and the diodrast clearance, a measure of tubular activity, was found to be within normal limits. These findings indicated a possible lowering of glomerular pressure. An explanation of this lowering of glomerular pressure was offered from the application of Poiseulle's law, a law relating to the physical behaviour of homogeneous fluids in rigid capillary tubes. The alteration in vascular tone which would produce a fall in glomerular pressure when the blood pressure in the renal artery was raised would have to be a constriction of the afferent arteriole out of proportion to whatever tone was present in the efferent arteriole. The height of the resistance in the afferent and efferent arterioles was arrived at by using a formula in association with Poiseulle's law, with allowances made for certain errors to allow for the application of the law to blood flowing through natural vessels. The total of these resistances was found to be increased in acute nephritis.

All this postulation was made on the assumption that two other possible explanations of lowered glomerular filtration were not present. These were: (1) a decreased permeability of the glomerular capillary wall, and (2) a shunting of the renal circulation as described by Trueta. Either of these conditions could account for the clearance-test results. A decreased permeability of the glomerular wall was rejected on the grounds that inflamed

capillary walls were more permeable and allowed the escape of albumin and red cells. On inulin clearance findings alone it might be said that there is decreased permeability. If there is obstruction to the small inulin molecule there must be a far greater impediment to the passage of the larger albumin molecule. I suggest, however, that on the assumption that there is a Trueta shunt of the circulation in acute nephritis, the vasoconstriction affects the cortical glomeruli, as well as their afferent arterioles. The resulting local diminution in blood volume and the effect of the centripetal forces associated with the vasoconstriction cause changes in the physical character of the cell walls of the glomerulus which prevent the escape of the protein molecules and, indeed, I think that the cortical area of the kidney is not associated at all with the production of albuminuria. The Trueta mechanism, which would explain the low inulin clearances on the grounds that some of the glomeruli were no longer fully perfused, was rejected on the grounds that the altered efferent circulation associated with the tubules would not be in keeping with the normal diodrast clearance findings. I cannot agree with their interpretation (and deductions) of this mechanism. The larger calibre of the efferent vessels of the juxta-medullary glomeruli, the projection of the loop of Henle deep into the medulla, and the intense medullary vascularity of the kidneys noted in experimental animals which give a picture possibly approximating to that of acute nephritis, would appear to me to be capable of providing a circulation in keeping with the diodrast clearances. The application of Poiseulle's law, even allowing for errors, appears to me to be too hypothetical to apply to such a dynamic structure as the kidney. It is of interest to note here that other investigators, applying clearance tests in cases of acute nephritis, noted *diminished tubular function and increased kidney blood flow; results quite opposite to Platt and his colleagues.* It is possible that the diversion of the blood flow from the cortex may provide an explanation for some of the apparent inconsistencies which have been noted by various workers in the results of renal function tests and renal blood flow. The phenomenon I have observed regarding the albuminuria would, I believe, be more in keeping with the findings of the Oxford school than the Manchester school.

SYMPATHETIC ACTIVITY AND ALBUMINURIA

The renal circulation in disease would not appear to have been noticeably studied from the variations in the degree of albuminuria. In a personal communication Professor Trueta tells me that Hamburger of Paris has produced albuminuria in animals by abnormal postures and prevented this by sympathectomy. It is of interest here to note that a study of albumin/globulin ratios may be of value, as providing a clue to alterations in the renal circulation. Where vessels are constricted the associated centripetal forces may alter the cell wall, even if diseased, in such a manner as to oppose the passage of the larger globulin molecule. Where vessels are dilated due to

increased blood volume the converse would hold. *Centrifugal forces* would assist the passage of the globulin molecule through the stretched cell wall.

The albumin/globulin ratio would be high where there is vasoconstriction and low where there is vasodilatation. This albumin/globulin ratio is low in orthostatic albuminuria which, in my opinion, is associated with a Trueta 'shunt' induced by abnormal sympathetic stimuli due to some spinal postural defect.

As a rule, there is complete recovery following an attack of acute nephritis. It is possible that certain changes in the renal circulation that have been assumed to occur during this disease have been considered as pathological rather than as a defence mechanism. Assuming that a shunting of the circulation does occur in acute nephritis, it would appear from available evidence to be associated with increased sympathetic activity. In the defence of the body the part played by the sympathetic nervous system is important. It might explain the usual recovery from such a catastrophic episode as acute nephritis. It may also explain the reported success of the use of antihistamines, which may act by increasing sympathetic activity. During an attack of acute nephritis a shunt of the circulation, while depriving the outer part of the kidney to some extent of a blood supply adequate for its nutritional needs, could at the same time ease the kidney from part of its work. This defence mechanism may at times be excessive, resulting in anuria and uræmia. It might therefore be presumed that this vasoconstriction could rest the kidney during the active state of the disease. In the treatment of anuria in acute nephritis it may therefore not be appropriate to adopt treatment causing prolonged interference with sympathetic activity.

THE INFLUENCE OF SLEEP ON ALBUMINURIA

The explanation of the phenomenon of albumin-free urine at night may now be attempted on the basis of the Trueta shunt mechanism. The degree of albuminuria depends upon the cellular damage allowing the passage of the protein molecule. This is influenced by the local blood volume and pressure in the capillaries concerned, and the systemic blood pressure. The area of the kidney to which the blood has been shunted, with its increased blood volume and local increase in centrifugal pressure, would be the main source of the albumin in the urine, this region of the kidney containing the juxta-medullary nephrons and associated circulation. A relaxation of this altered state of the renal circulation through decreased sympathetic activity, by a redistribution of the blood volume in the kidney and with a consequent lowering of centrifugal pressure, might temporarily result in a urine free of albumin.

A lowering of the systemic blood pressure could also contribute to this temporary state. Why this state occurs during sleep raises questions relating to the theories as to the cause and nature of sleep. Clinical and experimental observations point to the activity of the hypothalamus as of importance,

the hypothalamus also being considered the site of parasympathetic and sympathetic centres. Further, it has been argued that sleep is associated with increased parasympathetic activity and decreased sympathetic activity. Depression of sympathetic activity during sleep, with resulting decrease in local vasoconstriction and lowering of body blood pressure, might therefore be presumed to play some part in the production of albumin-free urine during an attack of acute nephritis. This hypothesis would be dependent upon the presence of a Trueta shunt mechanism in this disease. As a corollary I would suggest that this phenomenon might prove to be of favourable prognostic significance in acute nephritis.

SUMMARY

A clinical observation is noted which suggests the occurrence in acute nephritis of a defence mechanism associated with a shunt of the renal circulation as suggested by Trueta.

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USEFUL MANIPULATIONS IN GENERAL PRACTICE

By J. M. B. MORWOOD, M.B., B.Ch.

I practise with a partner. Between us we have about 6000 patients. Among this number I estimate that there are about 200 to 300 patients who have been relieved of (1) splitting headaches; (2) aching spinal columns; (3) sciatica; and (4) miscellaneous neuritic pains in the chest and abdomen. These patients have been relieved of their pains and aches by manipulation.

Since I began to manipulate my patients, I have learned by a process of trial and error to select my cases and also to manipulate in such a manner that, if I am not successful in relieving the patient, I do not offend him by causing severe pain without benefit. Also there is always the herniated or slipped intervertebral disc which must be borne in mind as a possible cause of the presenting symptom. Manipulation which compresses the herniated disc may cause very great harm. The manipulations which I use have a double safety factor. First, they are carried out without anæsthesia. Secondly, they have as an integral part of their nature a stretching of the vertebral column. Both these factors will prevent a herniated disc from being harmfully manipulated.

DOUBLE PATHOLOGY

With the exception of ruptured discs of various types, the pathology of fibrositis and neuritis is obscure. In my opinion, they are always the result

of a double pathology. Hypertensive patients do not always have headaches; the menses do not always cause backache; enteritis or the common cold do not always cause aching pains between the shoulders. In my opinion, the pains caused by these everyday diseases are due to an as yet unidentified lesion connected with the spinal column which the superimposed hypertension, menses, enteritis or coryza 'triggers off'. I understand that at least some of the 'trigger' diseases may cause a generalized disturbance of water balance in the body, and this hypothesis, if proved, may explain the mechanism of the double pathology. The object of spinal manipulation in general practice is to enable the patient to have raised blood pressure, her periods, diarrhœa or the common cold without severe neuralgia or pain.

It is on the basis of the double pathology of these conditions that both the medical profession and the osteopaths have gone astray in the past. Orthodox medical opinion, finding that headaches are a frequent associate of hypertension, tries to cure the headache by measures designed to lower the blood pressure. The osteopath, by manipulative measures, cures the headaches in many cases. He then states that the patient is cured because his symptom is relieved, or, if he likes to take more credit to himself, he says that he has cured a case of hypertension. So far as the patient's belief is concerned, the osteopath will more often be the better practitioner, as he will more often cure the symptom which made him seek treatment.

It is essential that the second pathology should always be looked for when a patient presents with a fibrositis or neuritis. Whether it is a cold or something more serious, it is usually desirable to treat it. Often it is better to wait until the general pathological condition has subsided before undertaking manipulation. Sometimes it is better to wait until the spinal as well as the general condition has settled. In this case manipulation merely prevents further fibrositis. The second pathology may have disappeared when the patient comes for treatment, as often occurs with influenza, and the fibrositis may then be more disagreeable to the patient than the influenza.

Fibrositis or neuritis is thus a very disagreeable condition caused by a 'triggering' disease. In the course of time, however, the condition will settle down without manipulation when the constitutional disease quietens down, or within two or three weeks of this happening, but when the next cold or influenza comes along, the neuritis or fibrositis may recur with all its previously disabling vigour.

SELECTION OF CASES

About 50 per cent. of cases of fibrositis and neuritis can, in my opinion, be cured by manipulation. Failures are due to:—

(1) Arthritis gumming the vertebræ together.

(2) Excessive muscularity, as in 'bull neck'.

(3) Muscular spasm, as in the nervous or frightened, or in the pain of recent date when 'Something slipped in my back as I bent down'.

(4) Excessive asthenia, when the vertebræ, if pulled into a reasonable alignment, immediately slip and twist again.

It follows from these reasons of failure that manipulation is most successful in children and young adults up to the age of thirty, but people of all ages may be cured.

Manipulation, when not contraindicated by the above conditions, is undertaken in the following circumstances:—

(1) When the spinous processes of the vertebræ are not in perfect alignment. This absence of alignment may sometimes be felt if not seen.

(2) When there is thoracic kyphosis, as in the asthmatic or asthenic type of individual.

(3) When migraine or occipital neuritis is associated with tenderness of the upper two cervical vertebræ. This neuritis usually has a sense of pressure or weight on the vertex of the skull. It also can be diagnosed by limitation of rotation movements of the skull.

(4) When a brachial neuritis is associated with a tender spot posteriorly at the root of the neck.

(5) When a thoracic neuritis ('Pain under the heart, doctor') can be traced along the line of a rib to a tender spot on the transverse process of the appropriate vertebra.

(6) When sciatica or lumbago is associated with tender spots about the lumbar vertebræ.

(7) When there is aching in any part of the spinal column.

(8) A few cases of neuritis respond to manipulation even though no tender spots can be traced. These are cases in which the second pathology is waning in intensity or, though present, is very slight.

METHODS OF MANIPULATION

The neck.—The patient sits in a chair with his back against the back of the chair from the sacrum to the shoulders. The manipulator stands on one side of the patient, places the hollows of the palms of his hands under the rami of the mandible and the tips of his fingers on the external occipital line of the occiput and stretches the neck, turning the chin towards the shoulder on his side, at the same time pushing the head slightly backwards. If this manœuvre is repeated several times with only a moderate amount of stretching force something may be felt to move in the cervical vertebræ in suitable cases. This procedure need not usually be unpleasant for the patient. The manipulation is then repeated from the other side of the patient, the head also being rotated to the new side. If the patient subsequently feels that his neck is freer and the amount of his voluntary rotation is increased, his headaches will probably cease.

The shoulders.—The patient sits across a chair with the back of the chair to either his right or left. The manipulator stands behind him. The patient locks the fingers of both hands together behind his neck and the manipulator,

passing his forearms in front of the patient's arms with the palms forwards, seizes the patient's wrists. In full expiration after an inspiration, the patient's arms are jerked up. In successful cases, a series of cracks are heard from between the patient's shoulders. It helps with this manœuvre to jerk up the shoulders with the operator's sternum in contact with the patient's back.

The lumbar spine.—The patient is placed lying on one side with the lower thigh in extension and the upper thigh in flexion. Both arms are in front of the body. The manipulator pushes the uppermost shoulder backwards with one hand and, with the other hand on the uppermost ilium, stretches and twists the lumbar spine by pushing the ilium sharply downwards and forwards. A satisfying series of cracks indicates success. Disc fracture is most common in the lumbar spine, so the extension part of this manipulation is very important; also, if it causes too much pain on a gentle try-out, it should be abandoned.

I have used other manipulations occasionally but seldom succeed with them when I have failed with these.

AUTOMANIPULATIONS

These three manipulations can be performed by the patient on himself. That for the neck can be performed by persistent rotation of the head up to the point of pain and then carrying out a nodding motion of the chin towards the shoulder. That for the shoulders can be done by locking the fingers behind the neck when sitting on a kitchen chair placed so that it cannot tip up. By raising the pelvis in the air, the full weight of the body comes onto the top of the back of the chair across the shoulders. The top of the back of the chair may be padded. The lumbar twist can be obtained by kicking one leg forward over the top of the other when lying face upwards in bed.

These manipulations are quite safe in all ordinary circumstances if intervertebral disc fractures are excluded. They cannot cause injury if they are carried out in such a manner that they do not hurt the patient, even in the presence of disc lesions.

SUMMARY AND CONCLUSION

Three methods of spinal manipulation are described which are believed to have removed annoying aches or distressing pains from about 5 per cent. of my patients.

There is a tendency when one is sure that no disc lesion is present to use enough force to upset the patient and hurt him. If this results in a cure, the patient bears no grudge. If, on the other hand, the patient is still left with his pain, unless he is of a thoroughly reasonable temperament he may subsequently receive his medical attention elsewhere. My partner now attends to several such. My successes always return to me. I do not include these failures among my 5 per cent., although in fact these patients have ceased to consult me about their neuritis.

CURRENT THERAPEUTICS

LV.—THE CHEMOTHERAPY OF TUBERCULOSIS

By J. V. HURFORD, M.D., F.R.C.P., D.P.H.
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In the last decade, a number of drugs, both antibiotic and chemically synthetic, has been received into the anti-tuberculosis armamentarium, and a still larger number has received the attention of laboratory workers. Exploration in the antibiotic field is always somewhat empirical, whereas the chemically synthesized drugs derive from those formulæ which are thought to be most likely to interfere with the essential metabolic processes of bacteria. The less recent members of both groups have been fully listed by D'Arcy Hart in his Mitchell lectures (1952). Of the many that have some effect on the *Mycobacterium tuberculosis* in the laboratory, few have achieved clinical use in man—the sulphones (e.g. promin, diazone, promizole), the streptomycin group, the thiosemicarbazones, *para*-aminosalicylic acid, calciferol, the Japanese drug, cepharanthine, and finally, isonicotinic acid hydrazide. The sulphones are now seldom used in tuberculosis and cepharanthine has not made its mark outside Japan; the field is therefore left to the five others. More effective substances than even the best of these are being sought and will probably be found in time, but compared with other infections it must be recognized that a very special problem is presented by tuberculosis.

SOME BASIC PROBLEMS

This problem resides in its intricate pathology, which demands that an ideal chemical should not only be bactericidal or strongly bacteriostatic in human beings, comparatively non-toxic and little inclined to produce drug resistance, but also capable of penetrating necrotic (caseating) lesions and the infected walls of lung cavities and of reaching intracellular organisms. In tuberculosis there is seldom an absence of necrotic avascular lesions in which the mycobacteria may be hidden alive, and they are often found within mononuclear cells. The antibiotics so far produced are water-soluble and likely to be evenly distributed in the body, but have shown no evidence of penetrative attributes. It is not surprising that they have all had maximum effect on lesions of lining membranes, e.g. laryngitis, bronchitis or enteritis, and within the lungs upon small hæmatogenous foci or spreading lesions still in the so-called exudative phase. Contrariwise, they have little influence on caseous areas in the lungs, solid organs or glands, and cavities which have reached a stage unlikely to be affected by changes in the bronchial anatomy.

It might be thought that if tuberculosis be diagnosed sufficiently early, the difficulty of inadequate penetrability would not arise. Unfortunately, any

case which has become capable of diagnosis probably has already a small necrotic lesion which may heal through natural resistance but not primarily through chemotherapeutic attack. In tuberculosis, perhaps, a large part of the beneficial effect of a useful measure is its encouragement of the resurgence of natural resistance which will be responsible for healing if this is going to occur. In such a chronic disease this must be so, and the fact suggests that time must be given for healing. Apart from an immediate bacteriostatic or bactericidal effect, an anti-tuberculous drug may possibly change cellular resistance directly. As allergy is a factor in the lesion, anything which can reduce it without lowering general immunity may be beneficial. Jensen (1949) suggested that streptomycin might have an anti-allergic effect, but this has not been confirmed. The thiosemicarbazones lower the reaction to tuberculin in direct skin experiments (Brandner, 1949), and work described recently by D'Arcy Hart (1952) on the combined anti-allergic and anti-tuberculous effects of certain surface-active polyoxyethelene esters is highly suggestive. Cortisone is also anti-allergic, but has other more dangerous effects (Spain and Molomut, 1950). Isonicotinic acid hydrazide is also reported to suppress tuberculin allergy (Steenken and Wolinsky, 1952). It seems likely that the effect of the main drugs in clinical use is on the *M. tuberculosis* itself. There has been uncertainty whether streptomycin is bacteriostatic or bactericidal, although laboratory experiments seem to point to the former action (Florey, 1949).

So far, the broad problems underlying the use of chemotherapeutic agents in tuberculosis have been discussed. More immediate to the clinical use of those which we currently possess are the problems of toxicity and development of drug resistance.

TOXICITY

Streptomycin and PAS are both comparatively non-toxic, the thiosemicarbazones much more so. The present low dosage of streptomycin has reduced the incidence of complications, especially of vestibular damage. Skin eruptions still occur in 2 to 10 per cent. of cases, and drug fever may lead to cessation of treatment, although it sometimes does not recur if a change is made to a different batch of streptomycin or to dihydrostreptomycin. The latter is less painful on injection and clinical results are similar to those of streptomycin. Whether or not dihydrostreptomycin can produce permanent damage to the auditory part of the eighth cranial nerve is still a matter for debate. Most instances reported have occurred when it has been used to treat tuberculous meningitis, although Romansky (1950) found that 33 per cent. of 115 patients treated with 2 (or more) grammes of dihydrostreptomycin developed deafness to speech or audiometer.

PAS notably produces intestinal symptoms, which can be reduced by giving it in an appropriate vehicle just before meals. They are not frequent, and in an institution where patients are given the sodium salt mixture as a

matter of course, there will be found few occasions for using expensive cachets or 'enteric-coated' capsules. More often than streptomycin, PAS can cause drug fever, and it may be necessary to desensitize with slowly increasing doses.

The thiosemicarbazones may have toxic effects on the liver (probably reversible), quite often produce a transient albuminuria, certain allergic manifestations and, uncommonly, blood changes, the worst of which is agranulocytosis. With doses of not more than 200 mg. a day, however, serious complications are unlikely.

DRUG RESISTANCE

The main problem has centred round the development of bacterial resistance to streptomycin, as this is still the most efficacious chemical weapon. Resistance to PAS can develop, but does so more slowly and less frequently. Despite anomalies in laboratory returns, resistance to streptomycin is assumed to be more likely the longer a course is continued, and thereafter to be permanent. As many as 85 per cent. of cases (*Med. Res. Coun.*, 1948) will have significant resistance after four months' treatment. Of the two theories, either of which would account for this, opinion is perhaps swinging towards that which postulates a change in the organism, rather than the favoured growth of insensitive mycobacteria already present. The clinical importance of the phenomenon is so great that there has been a tendency to reduce courses to not more than six weeks. The incidence is probably lowered if streptomycin is given intermittently (e.g., 1 g. every third day) (Tucker, 1949). It is now clear, however, that when there is combined administration with daily PAS, the likelihood of resistance is considerably less (*Med. Res. Coun.*, 1949). The minimum amount of PAS which will have this effect is not yet known, although a further Medical Research Council report on this aspect is now pending. Whether also, when PAS is badly tolerated, it can be replaced by thiosemicarbazone with similar effect is the subject of a recent, but as yet unreported, trial by the N.W. Tuberculosis Society. The safest conclusion is that whenever streptomycin is used in the treatment of a case with a pulmonary focus, it should be accompanied by administration of PAS; the rare exceptions to this would be acute miliary disease with intolerance to the latter drug and, perhaps, when the physician can safely anticipate complete control by the use of additional measures (which must not include resection).

CHEMOTHERAPY IN PULMONARY TUBERCULOSIS

The *thiosemicarbazones* have not established themselves in this country, nor has PAS alone. Either may be used when streptomycin therapy is withheld, and will have a slower and less certain effect on labile pulmonary lesions and on mucosal lesions. PAS is a safe drug and has been widely used in domiciliary treatment for reduction of positive organisms in the sputum

and improvement of symptoms in chronic cases. It is in just such cases, which may remain persistently or intermittently positive, that a public health problem will arise from the creation of streptomycin-resistant organisms. Alone, PAS may be given effectively in doses as low as 12 g. a day. 'Benemid'—a propylsulphanyl benzoic acid derivative—increases the plasma concentration of PAS (Boger and Pitts, 1950) and would thus reduce necessary dosage, but it may be doubted if such an addition to treatment is worth while.

In considering the use of *streptomycin*, certain points should be borne in mind:—

(a) Like all other agents fully tried out, it fails to sterilize necrotic foci and has its greatest effect on superficial lesions within the body or on exudative or hæmotogenous lesions.

(b) It is thus not a cure by itself, and usually must be fitted into a plan of treatment, so that it is best administered when a provisional plan can be made, preferably in a special hospital.

(c) It can shorten the duration of treatment and render safer the use of collapse therapy (especially artificial pneumothorax), so that few cases will be denied it at some time or another; but a short course is usually inadequate, and prolonged administration will allow of greater recovery of bodily resistance.

(d) Even with PAS, drug resistance may occasionally appear, so that when lung resection may be required, streptomycin should be held back to cover that operation and reduce the incidence of bronchial fistula.

Tuberculous tracheobronchitis and bronchitis play a large part in the pathology of phthisis. Ulcerative lesions seen through the bronchoscope respond well to streptomycin, and it is likely that pulmonary disease, especially cavities, may be altered through a similar effect. Deep-seated bronchial lesions also heal, and as they do, narrowing may occur, so that lobar or segmental atelectasis sometimes appears to result from streptomycin treatment. Quite often radiologically inactive phthisis of a chronic type is accompanied by intermittently positive sputum due to residual tuberculous bronchiectasis: in such cases all the current antibiotics can achieve negativity, which, however, may not last.

As regards dosage, the change from 2 g. to 1 g. of streptomycin daily resulted from experience of equal clinical effects and much less toxicity with the smaller amount. The further transition, now often made, to less frequent administration—to 1 g. every three days (twice a week)—was justified by the conclusion (Youmans, 1946) that *M. tuberculosis* reproduces in the test tube every $1\frac{1}{2}$ to $3\frac{1}{2}$ days, and is more susceptible to streptomycin when multiplying. Reports seem to show that 1 g. every three days is as effective as daily streptomycin over an adequate period and, with PAS, reduces the incidence of resistance even more than the latter plus PAS. Streptomycin every seven days has been reported to be as efficacious but slower in effect

(Furtos, 1950) and good results have been reported with 0.5 g. daily (Tucker, 1949). Speaking generally, however, either 1 g. daily or 1 g. twice weekly is the popular regime at the moment.

The introduction of means for controlling the risk of drug resistance has removed to a great extent the need for limiting the duration of treatment. It is realized that although improvement may be greatest during the first two to three months, it can continue while streptomycin is being given, or longer.

Streptomycin has not been found to exert any useful effect on primary pulmonary tuberculosis, unless there be bronchogenic or miliary spread, or active tracheobronchitis.

Isonicotinic acid hydrazide will be discussed later.

NON-PULMONARY TUBERCULOSIS

Meningitis.—The main problem here, if an effective chemotherapeutic agent be available, is to bring it in contact with the mycobacteria—often safely hidden in the thick exudate surrounding the mid-brain or choking the spinal subarachnoid space. In many cases an adequate course of streptomycin will lead to recovery without relapse, but the fact that this occurs in less than 50 per cent. of all cases, suggests that something more is needed. The chance of recovery depends upon the stage at which diagnosis is made and the presence or absence of tuberculosis (especially miliary tuberculosis) elsewhere. The basic dosage routine of streptomycin has become more standardized and depends upon high intrathecal concentration during the acute phase, reduced, but still effective, thereafter until danger of relapse is past. Streptomycin should be given intrathecally in doses of 25 to 100 mg. according to age and weight until the cerebrospinal fluid is normal, although it need not be given daily after the first two months if the changes are satisfactory. Intramuscular injections (20 mg. per lb. body weight [44 mg. per kg.], or 2 g. in an adult) accompany intrathecal therapy and are continued for at least three months after the cerebrospinal fluid has become normal (UNICEF, 1950).

Futher developments have concerned the more difficult cases. Spinal block may justify giving streptomycin by cisternal or intraventricular routes (Smith, Vollum and Cairns, 1948). Heparin and streptokinase have been used, not very convincingly, to prevent adhesions, but the most interesting development has been the employment of intrathecal tuberculin (P.P.D.) with streptomycin (Smith and Vollum, 1950). As resistance appears much less often than in pulmonary disease, PAS need not be given unless the latter also exists.

Miliary tuberculosis.—Here again, streptomycin is the drug of choice. A 50 to 60 per cent. recovery rate may be expected (*Med. Res. Coun.*, 1950). Adverse factors are the coexistence of chronic pulmonary tuberculosis or of meningeal involvement at the start of treatment. The occurrence of menin-

gitis later must be anticipated by examination of the cerebrospinal fluid, especially in acute cases or in those with poor response. PAS should be given to prevent streptomycin resistance.

Other tuberculous conditions.—In most other forms of non-pulmonary tuberculosis, streptomycin may be expected to give some assistance, especially when the condition is a 'surface' one (e.g. peritonitis, enteritis, cystitis). To a lesser extent, this is true of PAS and the thiosemicarbazones. In genito-urinary disease, the main effect is on mucosal lesions, but there is hope that a 'cover' with streptomycin in cases in which a kidney is removed for unilateral disease may increase the percentage of cures. In genital tuberculosis, the chemical agents have no very important place, although a trial of streptomycin in cases of endometritis (responsible for 6 per cent. of causes of sterility in women) is being conducted by the British Tuberculosis Association Research Committee. The treatment of bone and joint disease also has been little altered by streptomycin, except that it is again good operation 'cover', and as everywhere, tuberculous sinuses respond well.

OTHER CHEMOTHERAPEUTIC AGENTS

Neomycin, terramycin and viomycin.—These drugs have been isolated and tried out in the United States of America. Their main justification is their potentiality against streptomycin-resistant *M. tuberculosis*.

Calciferol (vitamin D_2), introduced by Charpy in France, and Dowling and Prosser Thomas in England, has proved especially valuable in lupus vulgaris and may cause over 50 per cent. recovery, although relapse is possible later. Better results are possible if streptomycin be given as well (Cornbleet, 1949). The dose is 150,000 units daily, and treatment must be prolonged.

It is probable that calciferol produces its effect through a different mechanism (as yet uncertain) from that of other chemical agents. With good response there is a replacement of tuberculous by young connective tissue. One striking effect is the occurrence of a focal reaction (with increased tuberculin sensitivity) ten to fourteen days after the start of treatment. Hypercalcæmia and renal damage must be watched for. Calciferol can be of value in superficial glandular tuberculosis and, more interesting still, in sarcoidosis—in which streptomycin also has been given good reports.

ISONICOTINIC ACID HYDRAZIDE

This, the newest of anti-tuberculous drugs, has received a good press. The hydrazide and an isopropyl derivative are being investigated in Britain under the ægis of the Medical Research Council. The former is a chemically pure synthetic substance of the general formula $C_6H_7N_3O$. The drug appears to have a narrow spectrum of potency against disease-producing organisms and to be of minimal toxicity. It is easy and cheap to produce and is administered by mouth. It is also quite slowly excreted from the body. These are almost ideal attributes, provided its promise be fulfilled.

In laboratory animals infected with tuberculosis it appears to have roughly a therapeutic effect equivalent to that of streptomycin.

So far, trials in man have been limited to patients with advanced disease, and the reports of these preliminary trials seem to indicate a reversal of the downward trend—reduction in fever and cough, gain in appetite and weight, reduction in organisms in, and in a few cases conversion of, the sputum, within a comparatively short period. Naturally in the type of case treated, although improvement in x-ray changes was reported, it could not be very marked (*Amer. Rev. Tuberc.*, 1952). In the presence of tuberculous meningitis, a high concentration has been reported in the cerebrospinal fluid following oral administration. Perhaps significantly, the drug lowers the response to the tuberculin test. It is also important that improvement in general condition does not appear to be mirrored by lowering of the erythrocyte sedimentation rate. The dose used is in the range of 3 to 5 mg. per kg. body weight (150 to 300 mg. per day for an adult). Reported side-effects are constipation, difficulty in starting micturition, increased reflexes, positional hypotension, eosinophilia, and slight lowering of hæmoglobin. These are unimportant, and if they do occur have not so far been very obvious in cases observed by me.

Many problems remain to be solved with regard to isonicotinic acid hydrazide, for instance, its effect on the bacillus (bacteriostatic or bactericidal), its effect on man (whether prolonged administration will cause toxic changes equivalent to those in laboratory animals), how best it can be used, whether drug resistant strains of the mycobacterium will emerge. Information on this last point is already beginning to emerge and is somewhat disquieting. A recent Veterans Administration report (1952) suggests that *M. tuberculosis* is *in vitro* capable of slow habituation to isonicotinic acid hydrazide, and in a few humans this effect was more rapidly achieved. R. Knox and colleagues (1952) report resistant organisms on subculture after as short a time as three to four weeks; moreover, their observations on corneal tuberculosis in mice show that the condition is only temporarily cleared by the drug.

The uncertainty as to the value of isonicotinic acid, and especially lack of knowledge about its capacity for bringing about drug resistance, should argue strongly in favour of limiting its use for the present outside of chest clinics and special hospitals.

It is possible that other compounds similar to isonicotinic acid will be found to have anti-tuberculous properties.

THE FUTURE

There is no doubt that the present era of antibiotics and synthetic drugs has revolutionized the treatment of tuberculosis, especially pulmonary tuberculosis and its complications. Fortunately, they have not been given the status of a definitive treatment, and indeed, firmly placed in the scheme of treat-

ment planned for the individual patient, have had the effect of raising our 'sights'. Even a decade ago, dealing with a well-established case of pulmonary tuberculosis was often a matter of salvage and patching-up, with prolongation of life rather than a cure as the result. Now, we hope for something more, and the chemotherapeutic agents have, like bodily rest, almost become basic to the more radical forms of treatment. Indeed, streptomycin has made possible the newest type of major surgery—resection of the whole or part of the lung.

Further agents will appear for trial and will be judged against the hitherto most effective—at present, streptomycin. Search will be made for other compounds of microbial origin, for chemical relatives of existing drugs and for other substances which resemble the essential metabolitites of the *M. tuberculosis*—greater research into which is certainly required.

Apart from improved antibacterial action, means to improve the penetrative attributes of new or existing drugs would be of great importance. According to Florey (1952), a drug with larger molecules than those at present in use might be taken up by phagocytes and pass through vessels neighbouring caseous foci, which are likely to have walls of increased permeability. The alternative now in the minds of clinicians is to increase the vascularity of tuberculous areas by the use of an ancillary drug which will produce a focal reaction. Tuberculin has been given subcutaneously for this purpose (Westergren, 1950), but so far no convincing results have been published. (Curiously enough, it has been found that quite heavy doses of tuberculin are necessary to produce a reaction in chronic phthisis.) Fielding (1951) has used calciferol with a similar idea in mind, but it cannot be said that the results are striking. Cortisone might be so employed but for the laboratory evidence of its danger in the presence of active tuberculosis.

In conclusion, it may be said that in tuberculosis we have an infectious disease which presents many more problems than those of a simple infection. Against the causative organisms, effective chemotherapeutic agents already exist which, though their influence on treatment has been profound, cannot by themselves be other than a limited offensive weapon in a very difficult campaign.

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EDITORIAL NOTE: Dr. Thomson, joint editor of *The Practitioner*, has just returned from the United States. He attended the National Tuberculosis Association conference in Boston, and the Annual Congress of the American Medical Association in Chicago. In the following article he presents the views expressed at this conference on isonicotinic acid hydrazide and his article provides an interesting postscript to Dr. Hurford's article on the chemotherapy of tuberculosis.

ISONICOTINIC ACID HYDRAZIDE AND TUBERCULOSIS

A PROVISIONAL ASSESSMENT

By WILLIAM A. R. THOMSON, M.D.

A RECENT visit to the United States of America, which included attendance at the annual meeting of the National Tuberculosis Association in Boston in May, provided an opportunity for obtaining the views of American workers on the present status of isonicotinic acid hydrazide and its derivatives in the treatment of tuberculosis. In this article an attempt is made to assess as objectively as possible what can only be described as a very confused picture.

PREMATURE PUBLICITY

There is universal regret at the premature publicity which was given to the use of isonicotinic acid hydrazide in tuberculosis. This has done nothing but harm. Not only has it raised the hopes of thousands of tuberculous patients that here at last was a 'cure' for tuberculosis, but it has also made it unnecessarily difficult for clinicians to organize adequately controlled clinical trials. Further, some of the original newspaper stories were so fantastic that the leaders in the tuberculosis field have to go out of their way to explain publicly that this new drug is not a 'cure' for tuberculosis and, indeed, that

'if not handled properly it could push back the tuberculosis control movement instead of advancing it'. How all this unfortunate publicity could have been avoided, particularly in a country where health, disease and drugs are all 'news' and 'news' is the salt of life, it is difficult to see. The problem, however, is rapidly attaining serious proportions and calls for careful consideration both by newspaper proprietors and editors on the one hand, and the medical profession on the other.

CURRENT CLINICAL ASSESSMENT

Although it is now nine months since clinical trials were initiated, the situation is still very obscure. One or two facts, however, are beginning to emerge. In the first place there is no doubt that isonicotinic acid hydrazide is an active anti-tuberculosis agent in man. How active it is, is still not known. The original New York workers are maintaining a more optimistic attitude than subsequent investigators. The Veterans' Administration, which is responsible for the treatment of all tuberculous ex-Servicemen, and which has therefore had an extensive experience of the chemotherapy of tuberculosis, is maintaining a more cautious attitude. Their provisional opinion is that the early results of treatment of pulmonary tuberculosis with isonicotinic acid hydrazide are no better than those with combined streptomycin and *para*-aminosalicylic acid (PAS) therapy. This is a view which is shared by the workers at the Trudeau Sanatorium. The general consensus of opinion among experienced clinicians in the tuberculosis field appears to be that, so far as it is possible to give an opinion at this stage, isonicotinic acid hydrazide and its derivatives are not as active as streptomycin. On the other hand they may prove to be of real value as an adjuvant to streptomycin, possibly replacing PAS, or even occasionally being given in conjunction with streptomycin and PAS.

This possibility is supported by the preliminary evidence from a controlled clinical trial involving 120 to 130 patients. One-third of these patients are being treated with isonicotinic acid hydrazide alone, one-third with this drug + PAS, and one-third with isonicotinic acid hydrazide + streptomycin. After four months' treatment the average gain of weight in these groups is 2.9 lb., 4.3 lb., and 6.4 lb. respectively, and the other beneficial responses to treatment are in the same proportion.

EUPHORIA, APPETITE, AND WEIGHT

One of the most striking features of isonicotinic acid hydrazide and its derivatives, reported on by the original workers and confirmed by subsequent investigators, is the systemic effect they produce, irrespective of any apparent direct action on the underlying infection. Within a relatively short period of initiating treatment, the patient develops a sense of well-being, his appetite increases, he puts on weight, and there is a reduction in cough, sputum and fever. As often as not, there is no corresponding im-

provement in the sputum or radiological picture of the lungs. The extent of this systemic improvement is well illustrated by the experience of the Trudeau Sanatorium:—

> In a series of 39 patients with 'advanced cavitary pulmonary tuberculosis and organisms resistant to streptomycin' treated with isonicotinic acid hydrazide (4 mg. per kg. body weight daily) for six to fifteen weeks, increased appetite was noted in 29, increased strength and well-being in 30, and reduction in sputum weight in 28. Gain in weight was not so marked in this series, but in seven it ranged from 11 to 26 lb.

Looking back, there can be little doubt that this euphoric action was, in part at least, responsible for the initial enthusiastic reports. It is a new phenomenon in the chemotherapy of tuberculosis and, whilst the physicians in charge of the trial fully appreciated its relative non-significance, in view of the minimal radiological changes, it is not surprising that the patients, many of them drawn from the strata of society graphically described by a New York physician as 'Bowery bums', and in advanced stages of the disease, should have been convinced that this really was a 'wonder drug'.

Although this effect of the drug is obviously merely incidental to the anti-bacterial action, it is clear that it is an effect which is not without value in the treatment of the tuberculous patient. If the patient's morale and appetite can be stimulated, this must play a not unimportant part in aiding his return to health.

TUBERCULOUS MENINGITIS

Another valuable property of isonicotinic acid hydrazide is the ease and speed with which it penetrates to all parts of the body, including the cerebrospinal fluid, following oral administration. This facility in penetrating the meningeal barrier has already been seized upon as a clue to the possible value of the drug in tuberculous meningitis. There is no question of isonicotinic acid hydrazide replacing streptomycin in the treatment of tuberculous meningitis, but preliminary results suggest that it may be a valuable adjunct to streptomycin in the treatment of this condition. Indeed, it is not impossible that a combination of isonicotinic acid hydrazide by mouth and of streptomycin intramuscularly may eliminate the necessity for the intrathecal administration of the latter in all but the more fulminating cases. Similarly, there are indications that streptomycin + isonicotinic acid hydrazide may be the treatment of choice in miliary tuberculosis.

DRUG RESISTANCE

All these hopeful prognostications, however, are conditioned by two ominous factors which are already causing considerable worry. The first, and most important, of these is that bugbear of the chemotherapy of tuberculosis—the devilish ease with which the tubercle bacillus can protect itself by developing a resistance to a new drug or antibiotic. How serious the problem is in the case of isonicotinic acid hydrazide, it is impossible to say

at the moment, but there is ample evidence that, when it is given alone, resistance can develop within a relatively short space of time. The Trudeau workers, for instance, report development of resistance in 11 out of 35 patients in whom the relevant data were available, and in one patient it developed as early as the twenty-sixth day of treatment. In some cases the development of drug-resistance was followed by bacteriological relapse. Comparable findings are reported by the Veterans' Administration, whilst Dr. Carl Muschenheim, Associate Professor of Clinical Medicine at Cornell University Medical College, who has had considerable experience with the drug[5], considers that the present evidence suggests that the development of resistance may well be the big limiting factor to the use of the drug. Dr. Nicholas D'Esopo, chief of the tuberculosis service, Veterans' Administration Hospital, Sunmount, N.Y., goes even further and states that he would not use isonicotinic acid hydrazide at the moment because of the risk of resistance developing; pending further information he prefers to adhere to the well-proven streptomycin-PAS combination. Dr. Walsh McDermott, on the other hand, who is editor of the *American Review of Tuberculosis* and was responsible for some of the original clinical trials, is not yet convinced that the development of resistance is a serious problem.

It may well be that, as in the case of streptomycin, a combination of isonicotinic acid hydrazide with one of the other proven anti-tuberculosis drugs or antibiotics may overcome this problem of drug resistance. Meanwhile, however, it is clear that, pending further authoritative information, the indiscriminate use of the drug should be deprecated.

TOXICITY

Here again the position is somewhat confused. Laboratory investigations suggest that in the dog toxic manifestations appear when the daily dose reaches 10 mg. per kg. body weight, and that they are a serious factor when the dose is raised to 20 mg. per kg. body weight. As the usual dose in man is around 4 mg. per kg. body weight, this does not allow a very wide margin of safety if the toxicity in man is comparable to that in the dog. On the other hand, no serious toxic effects have yet been reported in man, even among patients with tuberculous meningitis who have received as much as 10 mg. per kg. body weight. Indeed, one has heard of patients receiving as much as 25 mg. per kg. body weight for short periods, without apparent adverse effect. The side-effects which have been reported in man include: hyperreflexia, vertigo, constipation, muscular twitching, delay in micturition, urethral anæsthesia, paræsthesia of the extremities, dryness of the mouth, insomnia or restlessness, skin rashes, and transient loss of memory. In view of the predominantly neurological character of these side-effects, it is of interest to note that convulsions constitute the important toxic reaction in dogs.

The evidence so far available thus suggests that toxicity is not likely to be

a serious problem in short-term therapy. On the other hand, the treatment of tuberculosis is a long-term policy, and it will be necessary to wait until reports are available on the results of a large series of patients treated over a long period of time before giving a final opinion on this important aspect of therapy.

THE ISOPROPYL DERIVATIVE

The only derivative of isonicotinic acid hydrazide which has as yet been submitted to clinical trial is the isopropyl derivative, l-isonicotinyl-2-isopropylhydrazine. There is no doubt as to its anti-tuberculosis activity, but opinion differs as to its value relative to isonicotinic acid hydrazide itself. One group of workers has reported that it is more active. Another group, however, whilst finding that the isopropyl derivative appeared to produce earlier and greater gains in weight and reduction in sputum, found no difference between the two drugs in their effect on the bacillary sputum count or the X-ray changes. Further, the isopropyl derivative appeared to give a greater variety and frequency of side-effects. Clearly, more time is required to decide upon the relative value of the two preparations.

CONCLUSION

To be dogmatic at the present moment is unjustifiable, but two definite facts do appear to evolve from the available information. The first is that isonicotinic acid hydrazide is an active anti-tuberculosis drug in man and is deserving of full and careful clinical investigation. The second is that, pending such investigation, it should be used only under skilled medical supervision. To paraphrase an historic dictum, in tuberculosis the price of success is eternal vigilance.

The May 24, 1952, number of the Italian journal *Minerva Medica* is a special number on isonicotinic acid hydrazide, containing sixteen articles, many written in an optimistic vein, the first of which is by Prof. A. Omodei-Zorini, Director of the Istituto Carlo Forlanini in Rome. Among the topics discussed are the applications of the drug to pulmonary tuberculosis, including chest surgery, and to tuberculous laryngitis and bronchitis; the results obtained in experimental tuberculosis in the guinea-pig and in experimental ocular tuberculosis; and the determination of the drug in the urine. A case is described of a girl aged seven, with acute miliary tuberculosis, in whom the drug, assisted by streptomycin and PAS, appears to have brought about a cure. An article by G. Fegiz, Sub-Director of the Istituto Carlo Forlanini, carefully describes the complications encountered from using isonicotinic acid hydrazide in pulmonary tuberculosis.

REVISION CORNER

THE DIAGNOSTIC SIGNIFICANCE OF CYANOSIS

THE bluish colour of cyanosis is due to the presence of an abnormally high percentage of reduced hæmoglobin in the skin capillaries, and is usually most conspicuous in areas richly supplied with superficial blood vessels. It is of diagnostic value only when considered in conjunction with the patient's other signs and symptoms, and its assessment is made easier by dividing the causes of cyanosis into two main groups—central and peripheral. This distinction is important.

PERIPHERAL CYANOSIS

When the blood flow through the tissues is slowed, a longer time is available for the red corpuscles to give up their oxygen. An increased amount of reduced hæmoglobin is formed and cyanosis results. The blue colour is most conspicuous in exposed areas where the circulatory slowing is marked and superficial vessels present, i.e., the nose, cheeks, ears, hands and feet.

Local causes.—The most common cause of peripheral cyanosis is arteriolar constriction which reduces the capillary blood flow and renders the affected area cold and cyanotic. The vasoconstriction is usually due to cold or to undue sensitivity to cold, such as occurs in Raynaud's disease and acrocyanosis. Local cyanosis may also be caused by stagnation of blood in the capillaries due to venous obstruction. This is seen in the limbs after venous occlusion, and in the upper part of the body when the superior vena cava is obstructed.

Low cardiac output.—In conditions which cause a reduction in the cardiac output, the oxygen tension in the blood leaving the lungs is usually normal or only slightly reduced, but because the circulation is slowed and vasoconstriction often present, there is more time for oxyhæmoglobin to be reduced as the blood flows through the tissues. Hence peripheral cyanosis may be seen in shock, mitral or aortic valvular disease, and hypertensive or ischæmic heart failure. Some of the cyanosis in these cases may be of central origin, due to poor oxygenation of the blood as a result of pulmonary congestion.

Polycythæmia may occur in congenital heart disease and to a lesser extent sometimes in emphysema. The total amount of hæmoglobin in the blood is increased, and even if the proportion of this in the reduced state were normal, there is still excess *reduced* hæmoglobin present. Polycythæmia intensifies the blue coloration: the skin capillaries are distended by the increased blood volume and the circulation is slowed by the increased blood viscosity.

CENTRAL CYANOSIS

In cyanosis of central origin, blueness of the extremities may be marked, but characteristically there is in addition cyanosis of warm surfaces such as the conjunctivæ, the inside of the lips, the palate and the tongue. Central cyanosis is due either to failure of the blood to be oxygenated properly as it passes through the lungs, or to a congenital anomaly of the heart whereby some of the unoxygenated venous blood returning to the lungs is shunted into the systemic arterial tree without passing through the pulmonary vessels.

Respiratory disorders.—Failure of the blood to be oxygenated adequately in its passage through the lungs may be caused by a number of pulmonary disorders

which interfere with the entrance of oxygen into the lungs or its diffusion across the alveoli, and which are usually accompanied by dyspnœa at rest. In children, the air flow through the larynx or trachea may be obstructed by the presence of a diphtheritic membrane or a foreign body; dyspnœa is usually marked and stridor present. Spasmodic cyanosis and stridor are found during the paroxysmal laryngeal obstruction which occurs in whooping-cough, catarrhal laryngitis (spasmodic croup), and laryngismus stridulus (a manifestation of tetany seen in rickets). In poliomyelitis, dyspnœa and cyanosis may follow decreased pulmonary ventilation and accumulation of mucus due to progressive paralysis of the respiratory muscles. Asthma, severe purulent bronchitis, bronchiolitis and pneumonia may prevent oxygen entering the alveoli and cause dyspnœa and cyanosis, especially in children. Pulmonary reserve is so great that extensive disease of the lung parenchyma must be present before cyanosis occurs. In adults, emphysema, by impairing pulmonary ventilation, is perhaps the most common cause of cyanosis, which may be intensified by polycythæmia and especially aggravated by the superimposition of an acute respiratory infection. Engorgement of the pulmonary vessels occurs in mitral stenosis and in left ventricular heart failure. This may hinder oxygen exchange between the alveoli and red cells in the centre of dilated pulmonary capillaries. Seldom, however, is the blood leaving the lungs sufficiently unsaturated to cause detectable cyanosis, which in these cases is largely due to slowing of the peripheral circulation.

Congenital heart disease.—Cyanosis is a conspicuous and important feature of certain types of congenital heart disease. The pressure in the left auricle, ventricle and aorta is usually higher than that in the corresponding parts of the right heart; with a single abnormal communication, blood flows from the left (arterial) to the right (venous) side of the heart, and cyanosis does not result. When cyanosis is present at, or soon after, birth (morbus cæruleus) there is either such a large communication that venous blood mixes freely with arterial blood, or there is, in addition to an abnormal shunt, some associated lesion, such as pulmonary stenosis, which by raising the pressure in the right side of the heart forces blood into the left side. In other cases cyanosis appears only after feeding, crying, exertion or a superadded respiratory infection, which by elevating the pressure in the right side of the heart reverses the blood flow through the abnormal communication. Infants with congenital cyanotic heart disease are difficult to rear, and often develop clubbing of the fingers and toes. In childhood their exercise tolerance is usually severely limited and exertion intensifies the cyanosis by increasing oxygen utilization in the tissues. The most common congenital cardiac lesion causing cyanosis is Fallot's tetralogy, in which there is pulmonary stenosis, an overriding aorta, a high ventricular septal defect, and right ventricular hypertrophy. Over the pulmonary area there is a systolic murmur, often with a thrill. Squatting after exertion is a characteristic feature. These patients are particularly benefited by a subclavian-pulmonary artery anastomosis or other surgical treatment. Hence the importance of referring children with cyanotic heart disease to special centres for exact diagnosis.

ABNORMAL PIGMENTS

In rare instances the appearance of cyanosis is due to methæmoglobin or sulphæmoglobin. Methæmoglobinæmia may be a congenital defect and be confused with congenital heart disease. In adults, methæmoglobinæmia is usually due to

drugs, particularly acetanilide, phenacetin and sulphonamides. The pigment imparts a brown colour to the blood and is converted to hæmoglobin by giving 300 to 600 mg. of ascorbic acid daily.

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THE TREATMENT OF FIBROSITIS

MOST physicians agree that fibrositis is not a unique disease process, but a syndrome with many possible causes; also, that it is probably not an inflammation of fibrous tissue. The trouble is that no one *knows* anything about it. There are those who think they know; but what they really know is some hypothesis that more or less fits the observed clinical facts.

I would place patients with fibrositis broadly in two groups: (1) those in good health before the onset of their pain; (2) those in their usual ill-health. Any of the conditions mentioned in the immediately following section may be found in either group.

REFERRED SOMATIC PAIN

In recent years an increasing degree of credibility has been found in the idea that what was called 'fibrositis' in the past is often no more than referred pain from some localized pain stimulus in the deep somatic structures, and often outside the painful area.

Chronic sprain of an intervertebral ligament may be responsible; at the lumbosacral junction, for instance, it will cause 'fibrositis'—that is, referred pain and and tenderness—in the iliac crest area and down the outer side of the thigh on the same side. These cases of 'traumatic fibrositis' respond well, as a rule, to the repeated injection of 2 to 5 ml. of 1 per cent. procaine into the vicinity of the injured ligament.

A disc protrusion will cause the same diffuse pain and tenderness; so also will the *disc degeneration* not associated with the immobilizing paroxysms of protrusion. Disc protrusion demands *rest*, to the lumbar or cervical spine as the case may be. The immediate indication is for *rest in bed*. If pain does not abate in a reasonable time, rest for the lumbar region is achieved by a *short plaster belt;* for the neck by a *bi-valve neck plaster*. Disc degeneration presents a difficult therapeutic problem. *Short-wave therapy* to the affected region may be tried; and for the cervical spine, *traction* by a series of increasing weights, using special equipment.

Chronic postural strain of intervertebral ligaments is another possible operative lesion in fibrositis. Its treatment may be by *postural exercises;* or if the postural defect is one that cannot be corrected, it may be that relief can be obtained only by wearing a *belt* constructed to give lumbar or dorsi-lumbar support.

Theoretically there may be scores of lesions capable of causing the syndrome of fibrositis; many of them may be in the muscles or other soft skeletal tissues. It is only possible to speculate as to what they are.

FIBROSITIS AND AUTONOMIC INSTABILITY

I would now draw attention to a group of tired, ailing patients peculiarly liable to

fibrositis. As a typical instance, the disturbance of health likely to appear in women at the menopause may be cited. These weary patients 'ache all over'; they hate draughts, which bring acute discomfort to the back and shoulders; they have cold blue hands in the winter, and complain of a swollen, stiff, aching discomfort in fingers and feet in the summer; they complain bitterly of cold damp, or hot humid weather; they are continually ailing, with now one symptom now another —symptoms attributable to an instability of the vegetative nervous system. No treatment for fibrositis will bring lasting relief unless this underlying disturbance of health can be corrected. The following possible causal conditions of autonomic instability should be reviewed, and appropriate treatment instituted.

(1) *Anxiety and emotional disturbances.*

(2) *Focal sepsis.*—Far too much significance is still attached to this; but if teeth or nasal sinuses are clearly infected, treatment is, of course, advisable.

(3) *Spastic constipation.*—This condition is in itself a manifestation of vagotonia; but its successful treatment may bring relief from associated symptoms, including myalgia. Unfortunately, treatment of spastic colon is not very satisfactory. The patient should be dissuaded from regularly taking strong purgatives; one of the simple paraffin emulsions may be allowed. Normal bowel action is likely to be restored by *belladonna*, which may be prescribed, 5 to 10 minims (0.3 to 0.6 ml.) of the tincture, three times daily; and this may be combined with *bismuth* if the stools are loose and mucous.

(4) *The menopause.*—Hormone treatment of menopausal symptoms is essential if an associated myalgia and fibrositis are to be treated successfully. *Ethinyl œstradiol*, 0.02 mg. daily, may be prescribed, increasing week by week to twice daily or thrice daily until flushes have ceased; a slightly smaller dose may be continued for two or three months, then stopped by a gradual reduction. If there is clear indication of mild thyroid deficiency, *thyroid*, ½ to 1 grain (32 to 65 mg.) daily, should be given in addition.

Apart from these indications, the following physiotherapeutic measures are worth consideration:—

General ultra-violet light.—Nearly all patients benefit by a course of light treatment. The only exception is the highly strung, sympatheticotonic patient, who is sometimes made worse by it.

Sweating treatment.—This may be given by a radiant heat tunnel, or by various bath treatments. It is widely used, but its effect is a little uncertain. It should not be prescribed for debilitated patients.

Innumerable medicaments have been suggested for this form of 'muscular rheumatism'. Apart from the indications given above, and the analgesics, probably all are valueless. Aspirin, 5 to 10 grains (0.32 to 0.65 g.), or calcium aspirin, may be given three times daily for two or three weeks.

For the recurrent attacks of fibrositis from which these patients are so apt to suffer, *local heat and deep massage* is still considered to be of great value. But there can be little doubt that here also, much of the diffuse pain is referred pain and tenderness, the operative lesion being probably in the soft tissues, and possibly outside the painful area. Sometimes a zone where finger-tip pressure is severely painful and intensifies pain over the whole area can be found, in contrast to several others which are only locally tender. This is likely to be an important source of pain, and special attention should be directed to it. The notion, however, that there is something here which the physiotherapist must 'break up' by the

brute force of deep friction is probably a mistake. Firm, deep massage is all that is needed; or the zone may be infiltrated with 2 to 5 ml. of 1 per cent. procaine, and these injections may be repeated at intervals of a few days.

Treatment of areas of referred pain by massage is apt to prove disappointing.

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NOTES AND QUERIES

Head Lice

QUERY.—Can you tell me if there is a means of determining whether nits in hair are alive or dead? Often, after cleansing, a few nits are left, and they are considered to be alive and potentially dangerous, but I cannot find in the textbooks whether or not they can be tested to show they are definitely dead and harmless.

REPLY.—At the moment the egg comes from the female head louse (*Pediculus humanus capitis*) there is a flow of cement from glands which open into the oviduct; this cement glues the egg to the shaft of a hair and there is no substance in clinical use which will free the egg

Microphotograph to show larva pushing off 'cap' of nit.

from the hair. The eggs are attached normally close to the base of the hair. Nine days later the hatching larva pushes right off a cap which is formed at the tip of the egg and breaks out into the great big world. After the hatching, the empty shell may remain stuck to its hair, growing slowly farther from the scalp. The aim of treatment of pediculosis capitis is to put something on the head which will at the same time kill both lice and nits. Many things which do kill lice will not kill nits in the strengths used; however, the thiocyanate preparations and the 'gammexane' group are ovicidal, and one application of these will cure the infestation if the hair is not washed for ten days. DDT is not ovicidal but it is so persistent that it is probable that enough will remain to deal with all larvæ as they hatch out. A second application after one week would seem to provide complete cover.

If these views are accepted, there need be no anxiety about potentially dangerous nits; they will be but dead husks carried away from the scalp to be dealt with by the scissors or the comb of the hairdresser. Academically a differentiation has to be made between live nits on the one hand and dead or empty nits on the other. Live nits are smooth, firm, almost translucent, and when squeezed they pop. Dead or empty nits are flat and yellow. This difference can be better made out with the help of a hand lens.

(Your reader might be interested to read 'The Louse', by P. A. Buxton. London: Edward Arnold & Co., second edition, 1947.)

D. I. WILLIAMS, M.B., M.R.C.P.

Chronic Furunculosis

QUERY.—(1) In obstinate chronic furunculosis are injections of autogenous vaccines of any real value? (2) Has a course of tablets of stannous oxide any place in the treatment of such cases? If so what dosage is recommended? In the case in mind, the urine is negative for sugar and there is no evidence of serious underlying disease.

REPLY.—In obstinate chronic furunculosis, injections of autogenous vaccines are of real value in many cases, but some are refractory and do not respond to this treatment. Many years ago, I gave a prolonged trial to stannous oxide in the form of 'stannoxyl', but failed to see any advantage from this method of treatment. For many years, I have used a special form of toxoid originally made by Professor Dudgeon and myself. A recently isolated strain of *Staphylococcus aureus*, coagulase positive and hæmolytic, is grown for one month in beef broth plus

peptone. At the end of that time it is filtered through a Seitz filter and the filtrate is treated with 0.1 per cent. formalin. It is then put up in two dilutions, 1:10 and 1:100, with 0.5 per cent. carbolic saline. An initial dose of 0.2 ml. of 1:100 is given, and this is followed at weekly intervals by successive increasing doses until 1 ml. of 1:10 dilution is given. I usually wait until a furuncle is on the down grade before starting this course. If by any chance the initial dose is given from the 1:10 dilution, a sharp reaction is encountered, but I have rarely found any reaction from the small dose from the 1:100.

We have used this toxoid for many years, and although I have no statistical evidence I have found it very useful. There are, of course, still one or two intractable cases. It is interesting that we have had a number of patients who are well and free from boils so long as they are having the injections but tend to relapse when the injections are stopped.

J. BAMFORTH, M.D., F.R.C.P.

Immunity to Malaria

QUERY.—Until recently, I understood that immunity could occur naturally or be acquired only to infectious diseases caused by certain bacteria and viruses. During the past few years, references to 'immunity' and to 'hyper-immunity' to malaria have appeared in various articles. I should like to know: (1) What is the nature of immunity and hyper-immunity to the plasmodia which cause malaria? (2) How can it be detected in a given person? (3) Is it similar to immunity to bacterial and virus diseases? (4) Does immunity occur in any other disease caused by a protozoon?

REPLY.—Certain individuals are apparently naturally resistant to malarial infections and may live in endemic regions without acquiring the disease. Such subjects are considered to possess a high degree of natural immunity, which is presumed to be present before exposure to infection. Continuous infection or re-infection over a long period may result in the appearance of acquired resistance to the disease, which is usually referred to as immunity. This acquired immunity is chiefly concerned with resistance to re-infection with the strain of parasite responsible for the original infection (so-called super-infection). It is believed to develop as a reaction to the asexual erythrocytic stages of the life cycle of the parasite.

Immunity manifests itself in various ways. When there is continuous infection without clinical response, a state of tolerance is said to exist; residual infection associated with resistance to super-infection is called premunition. Immunity may be present without existing infection; for instance, it can be demonstrated for some time after radical cure. It appears to act mainly by stimulating phagocytosis and destroying the parasites, and not by inhibiting their division.

Appreciable resistance develops after a single infection only if the disease is allowed to progress for some time. It develops more rapidly after repeated infection. Effective resistance to a particular strain of human malaria is usually lost in a matter of months after adequate treatment. It is highly specific. Thus resistance to one strain of falciparum is often ineffective in protecting against infection from another strain even from the same or nearby districts.

The immediate bodily reaction to infection is the non-specific destruction of parasites, probably mainly by phagocytosis. Acquired resistance leads to a highly specific increase in phagocytosis, expecially in the spleen and liver. Antibodies are formed in the blood during malarial infection. Complement fixing, agglutinating and precipitating bodies can be identified in human malaria in two weeks or more after the clinical onset. It has been suggested that in malaria, and possibly in blackwater fever, the invaded erythrocytes are altered chemically by the parasite and become auto-antigenic; auto-antibodies are produced which, in combination with sensitized red cells plus circulating complement, give rise to hæmolysis.

Resistance to super-infection can be demonstrated in man or monkeys by experimental inoculation of known strains of parasites. The presence of humoral antibodies can be detected by the usual methods. The presence of acquired resistance is indicated clinically by modification of the attack following infection. In the indigenous population of an endemic area the disease is usually rare in young infants but common and severe in children, especially before the first year of life. So long as there is continued super-infection, malarial attacks in a given individual tend to become less severe as he grows older, and finally much modified and ameliorated in adult life. If infection is interrupted for some time acquired resistance rapidly weakens and the individual soon becomes subject to severe attacks. Such diminution of acquired resistance in communities is often the prelude to epidemics.

The mechanism of the production of immunity in malaria is not clearly understood. In some ways it resembles that in bacterial infections: for instance, the appearance of specific phagocytosis coincides roughly with the appearance of humoral immune bodies and with a reduction in electrical charge on the surface of erythrocytes which makes them more susceptible

to phagocytosis. In some forms of malaria the persistence of immunity seems to depend upon the continuous existence of the parasite. In others, this is not the case.

Immunity of a somewhat similar nature can be demonstrated in certain protozoal infections, including trypanosomiasis. By and large, however, the field of protozoal immunity is a difficult and somewhat neglected one.

PROFESSOR B. G. MAEGRAITH, M.B., M.R.C.P.

Infertility in the Male

QUERY.—A young married couple in their early thirties have had no children after five years of marriage. Investigation of the wife has shown no abnormality, but the report on the husband's seminal fluid reads: 'Volume 3 cc. Wet film shows only a very occasional spermatozoon (less than 1 per 1/6th field). Those present are either dead or only sluggishly mobile'. This examination has been repeated, and as it was done through our pathological service I assume the method of collection was reliable.

The husband was employed on special duties during the war in the forefront of the invading armies, and in enemy territory before the invasion of the Continent. He states that while on this work he was given special tablets which enabled him to withstand the constant strain and which also were said to abolish normal sexual appetite. He says that on demobilization his medical examination included examination of the seminal fluid. He had severe jaundice four years ago. I do not know the etiology of this. He has worked since the war in a hotel and now in a fashion shop.

The questions I wish to ask are: (1) Were tablets of this nature used? (2) If so, what were they? (3) Is there any treatment that will improve his sperm count and quality? (4) Can he be told, as he has requested, that no treatment will increase his sexual appetite, without at the same time holding out some hope of improving his fertility?

REPLY.—The tablets most likely to have been given in order to stimulate a man exposed to long fatigue and strain would be benzedrine, but these would have no lasting effect on sexuality. In any event, sexuality and fertility are different things, and the fact that the patient took these tablets has no bearing on his infertility.

The outlook for treatment is poor. The next step should be a testicular biopsy. This will reveal the state of the tubules and indicate whether or not they are sufficiently intact to make it worth while to attempt to stimulate activity by means of gonadotrophic hormones. The patient's insistence that if any treatment is given for his infertility, it must not stimulate his sexuality, is a curious one. A woman can conceive only if spermatozoa are present about the time of ovulation, and infrequency of intercourse is therefore quite a common cause of childlessness. Husbands are therefore more likely to ask for something that will stimulate desire rather than repress it. In any event gonadotrophic hormones do not stimulate desire.

KENNETH WALKER, F.R.C.S.

Breathing Exercises in Heart Disease

QUERY.—I understand that some cardiologists are of the opinion that certain types of breathing exercises carried out regularly, and often, tend to diminish the risk of coronary occlusion in later life. I would be grateful for your comments.

REPLY.—In so far as they may improve his general well-being and self-respect, breathing exercises may conceivabably postpone coronary occlusion in one prone to it, but there is no evidence of a direct effect in a particular individual. As part of general exercise, breathing exercises may promote general metabolism and perhaps reduce deposition of atheroma, but there are too many factors concerned in arteriosclerosis to justify a recommendation of exercise to one who does not feel the need for it.

C. J. GAVEY, M.D., F.R.C.P.

The Doctor's Wife as Secretary

QUERY.—I read with interest an article in the May issue of *The Practitioner* entitled 'The Doctor's Wife as his Secretary'. Could you please tell me: (1) Does the wife employed thus require to stamp a card under the National Insurance Acts? (2) How much is the stamp? (3) What benefits would she be entitled to under the National Insurance? (4) Would the income tax on her salary require to be deducted weekly under P.A.Y.E. scheme?

REPLY.—As regards National Insurance:—In the ordinary way, where a woman was employed the employer would have to pay 3*s.* 5*d.* and the employee 4*s.* by way of weekly contribution. An employee who is a married woman, however, is apparently exempt from the obligation to pay the 4*s.* Moreover, a woman who is employed by her husband is treated as a non-employed person, so that no contribution at all is payable by either the husband or the wife. The wife may, however, make a voluntary contribution of 4*s.* so as to entitle her to an *inter alia* retirement pension, which at present is 26*s.* per week but is expected to be increased. But the wife cannot be a voluntary contributor unless she was a contributor from the beginning of the scheme on July 5, 1952, or unless she has been employed or been self-employed for 52 weeks.

As regards P.A.Y.E., this applies irrespective

of the fact that the wife is employed by her husband, who should deduct the tax. If the pay is weekly or monthly, the husband must make remittances of the tax monthly. If the pay is quarterly, then the remittances would be quarterly. If, however, the pay does not exceed £3 per week, the husband need not trouble about P.A.Y.E., since the pay taken by itself would not attract tax, and, moreover, in such a case it is immaterial that the wife may have unearned income of her own.

T. J. SOPHIAN, *Barrister-at-Law.*

PRACTICAL NOTES

Bell's Palsy

THE result of a follow-up investigation of 209 cases of Bell's palsy is reported by R. Muller (*Acta Medica Scandinavica*, March 19, 1952, **142,** 284). Patients in this series were restricted to those who 'at the first admission had not reached the age of 40 years, and who had then paralysis of no more than 14 days' standing, of no recognizable cause, so-called idiopathic paralysis, and who according to examination and the history had no other signs of pathologic changes in the nervous system'. Six of the patients had died by the time of the follow-up; in no case was death due to a neurological cause. In the remainder the length of time between the onset of the palsy and the follow-up varied from ten to twenty years. Of the surviving 203 patients, 15 (7.4 per cent.) had had facial palsy before their first admission, and another 14 had a recurrence during the follow-up period. For an observation period of fifteen years the recurrence rate was 13 per cent. Two patients had had two recurrences during the observation period. In seven of the fourteen patients who had a recurrence during the period of observation the recurrence was on the same side of the face. Of the 29 patients with recurrent paralysis, 5 (17 per cent.) gave a history of other cases of facial palsy in the family; the incidence of familial history in those with only one attack was 4.6 per cent. During the follow-up period three patients 'had symptoms that may have been manifestations of disseminated sclerosis, but there was not sufficient clinical evidence to form a basis for this diagnosis in any of the cases'. The only treatment given was electrical stimulation, and 79 per cent. made a complete recovery, whilst another 18 per cent. had 'persistent but not inconvenient symptoms'. There was no disfiguration of the face in any of the cases. It is pointed out that 'experience has shown that no noteworthy spontaneous regression is to be expected after nine months. Therefore, operative procedures seem to be warranted if satisfactory restitution has not been obtained within this period of time'.

A New Mydriatic Combination

IN the course of an investigation of retrolental fibroplasia in premature infants, difficulty was found in obtaining efficient dilatation of the pupils. This problem was finally overcome, according to C. Reiter (*American Journal of Ophthalmology*, March 1952, **35,** 412), by the use of a mydriatic consisting of 'five per cent. phenylephrine hydrochloride, five per cent. eucatropine hydrochloride, one per cent. methyl cellulose, in a diluent of 0.45 per cent., sodium chloride'. The high viscosity of the solution results in its remaining in the conjunctival sac 'despite crying and the profuse production of tears'. The solution remains stable for at least two months. Slight discoloration may occur but this does not detract from its effectiveness. Marked discoloration causes irritation, but this degree of discoloration does not occur in under two months. It was used with success in an unselected group of 75 premature infants, one drop being instilled every fifteen minutes for three doses. Maximal mydriasis was attained within half an hour of the third instillation. The duration of action varied between four and six hours. Equally good results were obtained in 100 adults; here one drop gave maximal dilatation in one hour, with a duration of action of four hours. There were no side-effects.

Pre- and Post-Operative Treatment with Furacin Vaginal Suppositories

FURACIN vaginal suppositories have been used pre- and post-operatively in 90 cases of operations on the cervix and vagina by J. Schwartz (*American Journal of Obstetrics and Gynecology*, March 1952, **63,** 579). The operations included 39 cervical, 25 vaginal, 23 total abdominal hysterectomy, and 3 radium treatment of the cervix for carcinoma. Furacin vaginal suppositories contain 0.2 per cent. furacin dissolved in a self-emulsifying, water-miscible base of glyceryl laurate, 10 per cent., and a synthetic water-dispersible wax, 89.8 per cent. The method adopted was:—

(1) In 32 cases of post-electrosurgical treatment of the cervix, a furacin suppository was inserted into the vaginal canal and held in place with a tampon after the cervix had been cauterized. The tampon was removed the next morning, and the patient given a vinegar douche, after which a furacin suppository was again inserted into the vagina. The procedure was repeated twice daily, morning and evening. In all cases the cervix healed rapidly and cleanly within three weeks.

(2) In 25 cases of vaginal operations, furacin suppo-

sitories were inserted twice daily two days before operation. A vinegar douche was given on the morning of operation, and forty-eight hours postoperatively, after removal of the packing, a vaginal suppository was inserted daily. There was more rapid healing, decreased postoperative infection, reduced amount and odour of vaginal discharge, and removal of irritation.

(3) In 23 cases of total abdominal hysterectomy the same preoperative treatment was carried out twenty-four to forty-eight hours before operation, and twenty-four hours after operation daily insertion of furacin suppositories. 'The vaginal vault was well healed in 6 to 8 days, with a noticeable decrease in the postoperative vaginal bloody discharge.'

(4) In 3 cases of post-radiation treatment of carcinoma of the cervix, within forty-eight hours of removal of the radium a furacin vaginal suppository was inserted into the vagina twice daily after vinegar douching. The treatment was continued for two to three weeks, in some cases reduced to once daily. A marked reduction in amount and odour of vaginal discharge was noted, and the patient experienced a 'soothing sensation in the vagina. . . .'

No untoward reactions were noted in the 90 cases apart from slight vaginal irritation in one case after eight days' medication. In conclusion it is stated: 'Furacin suppositories . . . contribute to a smoother postoperative course in both vaginal and cervical surgery . . . they reduced the healing time and markedly decreased the slough and malodorous discharge'.

Hazards of Intravenous Administration of Iron

IN an editorial in the *Annals of Internal Medicine* (February 1952, **36**, 694) it is pointed out that 'it now seems certain' that hæmosiderosis can be produced by 'the excessive or protracted parenteral administration of iron'. After a review of the metabolism of iron in the body, and the genesis of hæmosiderosis, the conclusion is reached that 'iron should not be given intravenously to patients with refractory anæmia because they are refractory on oral administration, but only to those who have a hypochromic anemia with iron deficiency. It should not be given in a quantity materially greater than is needed to replace this deficiency, as calculated from the amount of hemoglobin and the probable blood volume. With this precaution, intravenous administration of iron should be valuable in a small selected group in whom iron orally administered is disturbing or poorly absorbed, and in the later stage of pregnancy, when rapid replenishment of the iron stores is important'.

'*Gammexane*' *Larvicide* (*Benzine Hexachloride*) *as a Rodenticide*

FOLLOWING upon the finding that when 'gammexane' larvicide (I.C.I.) was used in native huts for the control of ornithodorus ticks, rats were found dying in the huts after dusting with the powder, tests were carried out by G. R. Cunningham van Someren (*East African Medical Journal*, March 1952, **29**, 107) to estimate the rodenticidal properties of gammexane larvicide. Different species of rats common in the Nairobi district were caught and housed in cages, and after two or three days a number of tests were carried out, including light and heavy sprinkling of gammexane on the floors of the cages ; or the animals were made to pass along a runway filled with various soils treated with gammexane, or were left on treated surfaces for thirty minutes, or ran daily on such surfaces. Gammexane was also mixed in maize meal as a bait. In the first two tests in which gammexane was sprinkled on the floor of the cages or the animals were made to run once through a treated runway, mice were used. In the first (with the sprinkled floor) all the mice were dead within 108 hours; in the second (the runway) the majority were unaffected. Rats were used in the further tests: of 5 *Arvicanthis* submitted to three tests with wet soil runways treated with 0.5, 1 and 2 g. gammexane, one animal died at 156 hours and a second at 264 hours; the remaining were given treated food and all died, the last at 108 hours after the meal. A test with 4 *Rattus* species resulted in the death of all animals within 180 to 276 hours. A number of other tests were carried out with similar results. From the results of the tests it is estimated that 'gammexane is a rodenticide which may be of considerable practical value' . . . 'the quantity of gammexane required to kill a rodent, particularly by the oral route, is relatively small'. The possibility of the value of gammexane as an anti-plague measure is discussed: 'The practical application is visualized as a general dusting campaign in huts or buildings where plague or rodents occur'. The *Arvicanthis* species appeared to be more resistant to the toxic properties of gammexane, but 'nevertheless, this species will succumb if given sufficiently high concentrations, either by ground dusting or in bait'.

Rectal PAS Therapy

A REPORT on the administration of PAS per rectum, by drip enema, comes from E. Attinger (*Praxis*, April 3, 1952, **41**, 285). A 5 to 10 per cent. solution of the sodium salt was employed: to begin with for a few days 15 g. in 300 ml. of water, then 20 g. in 300 to 400 ml. water, twice daily, morning and evening. In order not to overload patients with marked cardiac dyspnœa, 10 g. in 100 ml. of water were given four times daily. In some cases treatment was continued for three to four months without interruption. Tolerance in all 16 cases in which rectal administration was employed for at least ten weeks was good. After three months' treatment intestinal pain occurred in two cases; sensitivity to the usual dosage occurred after three months in one case but disappeared after

the dosage had been adjusted to 30 g. in 5 to 10 per cent. solution. With this raised dosage there was a slight increase in the blood curve which righted itself after interruption of treatment for a few days. Two patients in the series had slightly increased diuresis. The indications for the use of rectal administration are stated to be all cases in which prolonged PAS administration is necessary, and in those cases in which oral administration is badly tolerated. Advantages claimed for the method of administration are the continued maintenance of a therapeutically active blood level, good tolerance, and undisturbed feeding. On account of marked individual variations in absorption the PAS blood level must be carefully controlled, and if with increased dosage the blood level does not become therapeutically active, continuation of the therapy is useless.

Neisseria in Genital Tract

FULL identification of *Neisseria* found in cultures from the genital tract of 1,575 patients has been attempted by A. E. Wilkinson (*British Journal of Venereal Diseases*, March 1952, **28**, 24). The patients were divided into three groups: Group A consisted of 1,095 female patients, in 204 of whom cervical secretions were examined, whilst in the remainder cultures were made from cervical, vaginal, and rectal secretions. Group B consisted of 130 men complaining of urethral discharge. Group C consisted of 350 patients attending an antenatal clinic, in whom urethral and cervical secretions were examined. The results were as follows :—

Group		A	B	C
Patients in group		1,095	130	350
Patients in whom *Neisseria* were found		290	68	2
Gonococci (fully) identified)	No.	251	63	—
	Per cent.	86.6	92.6	—
Presumptive gonococci	No.	29	4	—
	Per cent.	10.0	5.9	—
Neisseria other than gonococci	No.	10	1	2
	Per cent.	3.4	1.5	—

In other words, '3.4 per cent. of *Neisseria* isolated from female patients attending a Venereal Diseases Clinic were found not to be gonococci. The corresponding figure in male patients was 1.5 per cent.'. It is pointed out that these non-gonococcal *Neisseria* 'constitute a possible source of error in the bacteriological diagnosis of gonorrhœa. Any laboratory which undertakes cultural examinations for the gonococcus should be prepared to attempt its full identification by fermentation reactions and should not be content with any less stringent criteria'.

Glutamic Acid in Mentally Defective Children

THE effect of glutamic acid in 16 mentally defective children has been investigated in Sweden by V. Oldfelt (*Journal of Pediatrics*, March 1952, **40**, 316). The children, whose I.Q. ranged from 42 to 77, were aged seven to fifteen years, and were inmates of a children's home. The dose was 18 g. daily of 'granulated l (+) glutamic acid, given thrice daily in divided doses, and this was given for a period of just over four months. A control group of 15 comparable children was given a granulated substitute'. The treatment had no 'demonstrable effect' upon the intelligence quotient. 'Even though a somewhat greater tendency to improvement was evident in the glutamic acid group, it was probably too slight to have any value in such a small series'.

Coca-Cola in Excretion Urography in Children

FOR children over the age of sixteen to eighteen months the following technique is recommended by O. C. Berg and D. H. Allen (*Journal of Urology*, March 1952, **67**, 393). Fluids are withheld from the evening feed until the morning of examination. After a preliminary antero-posterior film, 10 or 20 ml. of 50 per cent. neoiopax are injected intravenously. During the next five minutes the child is given 6 to 12 ounces of Coca-Cola. Films are then taken five, ten, fifteen and thirty minutes after the injection. It is stated that 'this type of procedure is well tolerated, is simple and produces greatly improved excretory urograms. . . . In some instances, the use of Coca-Cola has provided pelvic, and calyceal outlines comparable in quality to retrograde pyelograms'. This technique is a modification of Matthei's technique (*J. Urol.*, 1950, **64**, 417), substituting Coca-Cola for milk. The authors have found that the Matthei technique is preferable for children and infants under the age of sixteen months, as in the latter group there tends to be ' "burping" with the consequent escape of the necessary gaseous medium' when Coca-Cola is used. In the Matthei technique 8 ounces of the infant's normal food, or, in older children, 8 ounces of milk or chocolate milk are given immediately after the injection of the contrast medium. In both cases 'the ingested material distends the stomach which in turn displaces the colon and small bowel leaving an unobstructed and undistorted view of the kidney structures through the gastric shadow'.

REVIEWS OF BOOKS

Tubercle Bacillus and Laboratory Methods in Tuberculosis. By M. A. Soltys, Ph.D., C. A. St. Hill, M.B., Ch.B., and I. Ansell, M.D., M.R.C.P. Edinburgh: E. & S. Livingstone Ltd., 1952. Pp. vii and 212. Figures 12, some in colour, Price 20*s*.

The three authors are to be congratulated on having produced such a clear and compact reference book, the reading of which serves to remind one of the enormous volume of historic and current investigation relating to the many aspects of the tubercle bacillus. To condense this literature into some two hundred pages is no light undertaking; the present work is documented by over seven hundred references to some five hundred authorities, and the writers regret the omission of many others. Few workers engage on more than a limited field, hence the wide scope of the book renders it useful as a compact *vade mecum*, and particularly helpful as a starting point for those wishing an entry to the literature on some specific topic. The tripartite authorship is sound, leading to more authoritative writing on the diverse fields covered, but it has often been difficult for the authors to strike the balance between adequacy of review and the expression of their own experiences and opinions as to the most appropriate methods to use; generally, stress has been laid on the former, thus making the book relatively impartial in its approach. The first part deals with general topics, such as history, morphology, chemistry, growth, and virulence, a subject in which the primary author is experienced; and the second part, written in conjunction with the collaborators, covers the standard techniques of laboratory investigations. The selection of methods is always personal to each laboratory, but the authors seem unaware, for example, of the proved advantage of the morning specimen (as opposed to 24-hour) when conducting urine examinations; and although eighteen routine culture media are described, the simplicity of a solid media technique for slide culture is overlooked. It is curious too, in a book frontispieced by Stanley Griffith's photograph, to find no mention of the relative distribution of human and bovine bacilli in various anatomical types of diseases, and histological examinations other than tissue stains for bacilli are unmentioned. The erythrocyte sedimentation rate and hæmograms are described but the absence of some mention of the Day's sedimentin index, the classic von Bondsdorf, and more recent Houghton indices introduces a minor imbalance; on the other hand the electron microscope, hæmagglutination and cyto-chemical tests all receive mention. The book should, however, prove a most useful addition to the shelves of the practising bacteriologist, who will also find the very full author and subject index a further convenience. No sanatorium should be without a copy.

The Ciba Foundation Colloquia on Endocrinology. Volume I. Edited by G. E. W. Wolstenholme, O.B.E., M.B., B.Ch. London: J. & A. Churchill Ltd., 1952. Pp. xx and 315. Figures 48. Price 30*s*.

This book is the first of a series of four recording the proceedings at Symposia held at the Ciba Foundation on various aspects of endocrinology. The first two volumes will deal with the steroid hormones, and the first one, divided into two parts, deals first, with the steroid hormones and tumour growths, and secondly, with steroid hormones and enzymes. This volume will be of great value to research workers in this large field, but it is outside the interest of the average man engaged in practice. There are, however, sections of general interest on the more clinical aspects of steroid hormones and cancer, the action of ACTH and cortisone in acute leukæmia in children, and the uses of massive doses of œstrogens in cancer of the breast and prostate. Unhappily no great therapeutic advance can be recorded.

Psychiatry in General Practice. By C. A. H. Watts, M.D., D.Obst.R.C.O.G., and B. M. Watts, M.B., B.S. London: J. & A. Churchill Ltd., 1952. Pp. viii and 228. Price 12*s*. 6*d*.

In this book Dr. and Mrs. Watts have described clearly and yet scientifically the psychiatric problems which face the general practitioner in everyday practice and have explained at some length how these arise, how they should be treated, and what results one could expect from direct and somewhat superficial methods. Anxiety states, neurosis, melancholia and hysterical reactions are given most attention, but there are excellent chapters on disturbances in childhood and in the aged. The authors have succeeded in simplifying diagnosis and therapeutic technique, but at the same time the descriptions do not suffer from the ignoring of the psychological mechanisms involved. This book is eminently readable and practical and can be recommended with every confidence to the general practitioner or even the specialist, whether his interests lie in psychiatry or not.

Those who are interested will find much helpful material, and those to whom the subject is alien cannot fail to find a new interest in their so-called functional patients.

Endoscopy. By EDWARD B. BENEDICT, M.D., F.A.C.S. London: Baillière, Tindall & Cox, 1951. Pp. xiv and 373. Figures 130. Price 76*s*. 6*d*.

EDWARD BENEDICT has probably contributed as much to the practice of endoscopy as any other man. His work has been done at the Massachusetts General Hospital where he holds the post of endoscopist to Harvard Medical School, and this book describes his present views. It is well written and profusely illustrated with X-ray reproductions and coloured pictures.

This book, which is prefaced by Edward Churchill, seeks to show that the specialist endoscopist has established his worth as a member of the staff of a teaching hospital. The author believes that by describing the disease processes which the endoscopist may meet, *before* he describes the technique of endoscopy, he will set the science on a sound footing. The result is that most of this book is made up of a series of brief accounts of a wide range of diseases—namely, those which afflict the bronchi, the lungs, the stomach and peritoneum. These accounts are misleading in their simplicity and it would seem that greater details of the techniques of endoscopy might more usefully have been presented. The author's references are numerous, but almost exclusively American. He makes no mention of Negus or Brock, who have done much to advance the value of bronchoscopy in recent years; he apparently is not familiar with the work which Allison and Johnstone have done to clarify the pathology and treatment of diseases of the œsophagus; and the contributions of Hermon Taylor and Avery Jones to gastroscopy receive but scant attention.

Clinical Radiology of the Ear, Nose and Throat. By ERIC SAMUEL, M.D., F.R.C.S., F.F.R., D.M.R.E. London: H. K. Lewis & Co. Ltd., 1952. Pp. viii and 339. Figures 320. Price 70*s*.

THIS is a handsome book which deals exhaustively with its subject. The positive reproductions of x-ray pictures are clear and informative. Diseases of the œsophagus are not included, the author stating 'the prime interest in that structure lies in its intrathoracic course and this aspect is fully covered in texts on thoracic and gastro-intestinal pathology'. In recent years the value of x-ray examinations in demonstrating the extent of lesions in the pharynx and larynx, particularly malignant disease, has been more fully recognized. Tomography is often of the greatest help. These aspects are well recounted and illustrated. It is interesting to find a chapter devoted to the radiology of the postoperative mastoid. Radiography of the nasal air sinuses is adequately described, and the appearances in infections and allergic states and other diseases are thoroughly dealt with. The author is level-headed and is not prepared to read too much into x-ray findings. Altogether the book should prove most useful to those interested in the subject.

Clinical and Rœntgenologic Evaluation of the Pelvis in Obstetrics. By HOWARD C. MOLOY, M.D., M.Sc. Philadelphia and London: W. B. Saunders Company, 1951. Pp. xi and 119. Figures 68. Price 12*s*. 6*d*.

THIS book provides a summary of its subject in the manner of the modern small American monograph. Dr. Moloy and his work are so well known that its contents are authoritative. It is a book for the specialist obstetrician rather than for the practitioner, although anyone wishing to reflect on his experiences of forceps deliveries will find much material to make him think. We note that this is the first of a series of such monographs on specialized medical subjects. If the others are as good as this one in content and production both authors and publishers may be congratulated.

Henry VIII: A Difficult Patient. By SIR ARTHUR SALUSBURY MACNALTY, K.C.B., M.D., F.R.C.P., F.R.C.S. London: Christopher Johnson Publishers Ltd., 1952. Pp. 200. Illustrated. Price 18*s*.

THE enigma of the personality of Henry VIII is one of the most intriguing in the history of these Islands. Which was the real Henry—the bluff King Hal of the early years or the Bluebeard of the latter years? Sir Arthur MacNalty has gone far towards solving the enigma in this book, the purpose of which, in his own words, is 'to demonstrate that the problem of King Henry's behaviour is more complex than the extremists on either side have assumed, and that his state of health and illnesses are of greater importance than has been supposed in the estimation of his rule and policy'. The dominating feature of his medical history was a varicose ulcer which developed at the age of thirty-six and which continued to trouble him throughout

the rest of his life, mainly because he persistently refused to obey his doctors' orders to rest his legs. It was not only responsible for repeated attacks of toxæmia resulting from toxic absorption, but was probably also responsible for a severe pulmonary embolism in 1538. Sir Arthur MacNalty can find no convincing evidence to support the popular story that the King had syphilis. In addition he had two severe head injuries in tournaments—one in 1524 and the other in 1536. Sir Arthur has 'no intention to explain, as some psychiatrists would do, Henry's tyranny, heartlessness and cruelty on medical grounds alone. There was evil in the man', but these 'maladies certainly helped to bring out the evil that a saner mental disposition would have controlled'. This is a fascinating book which will appeal to both doctors and historians. It is a brilliant interpretation of a relatively meagre medical record, carefully correlated with the life and actions of one of the outstanding figures in English history.

NEW EDITIONS

THE tenth edition of *Textbook of Medicine*, edited by Sir John Conybeare, K.B.E., D.M., F.R.C.P., and W. N. Mann, M.D., F.R.C.P. (E. & S. Livingstone Ltd., 37*s.* 6*d.*) has been subjected to extensive revision and two chapters have been rewritten by new authors, namely that on 'infectious fevers', by Dr. Thomas Anderson, and the chapter on 'tropical and helminthic diseases', by Lieut.-Col. W. H. Hargreaves. In addition there is much new material—on congenital heart disease, anticoagulant drugs, enuresis, congenital hæmolytic disease, and a new appendix on the sulphonamides and antibiotics. In his preface the senior editor deplores the necessity for the increased published price owing to the rise in costs since 1949, but the price is still moderate.

Diseases of the Nervous System, by F. M. R. Walshe, M.D., D.SC., F.R.S., in its seventh edition (E. & S. Livingstone Ltd., 24*s.*) contains new information on demyelination in connexion with the etiology and pathology of disseminated sclerosis, and also in relation to acute encephalitis. In the chapter on epilepsy there is a section on the use of 'tridione', and reference is made to the good results obtained by the administration of benzedrine in narcolepsy. In the section on acute poliomyelitis emphasis is laid on the rôle of trauma in the occurrence and site of paralysis, and it is pointed out that in the preparalytic stage even lumbar puncture may turn a non-paralytic into a paralytic case. Written largely for the use of practitioners, the new edition of this well-known treatise is assured of a warm welcome.

The Pathogenesis of Tuberculosis, by Arnold R. Rich, M.D., now appears in a second edition (Blackwell Scientific Publications, £5 7*s.* 6*d.*), for the preparation of which the author says the entire book has been carefully re-read for a search of any areas on which new information warranted amplification or modification of the views expressed. A revision of this classic work, indispensable to anyone interested in tuberculosis, is most welcome, but a number of quite important developments since the first edition appeared in 1945 receive rather scant attention. The discussion of B.C.G. vaccination is based almost entirely on evidence produced more than ten years ago. There is no reference to the effect of cortisone on experimental or human tuberculosis; indeed the word 'cortisone' does not appear in the index, and there is no reference to recent work by Bloch on the virulence of tubercle bacilli. Although the book cannot be relied upon as a guide to modern literature, its profound analysis and discussion of all the factors concerned with the pathogenesis of tuberculosis remain as valuable as ever.

Tests for Colour-Blindness, by S. Ishihara, M.D., in its tenth edition (Nippon: Isho Shuppan Co. Ltd.; London: H. K. Lewis & Co. Ltd., 75*s.*) is a welcome new and completely revised presentation of this well-known and standard test for colour-blindness. There are 6 new plates, although the fundamental basis of the test is unaltered. This consists in the application of the fact that to the red-green blind, blue and yellow are remarkably bright by comparison. Whilst it is true that full examination of the colour sense can only be made by spectroscopic or anomaloscopic methods, the Ishihara test provides a sound introductory clinical method; further inquiry can be made by one of the lantern tests in doubtful cases.

Emergency Surgery, Part IV, by Hamilton Bailey, F.R.C.S., F.A.C.S., F.I.C.S., F.R.S.E., in its sixth edition (John Wright & Sons Ltd., 21*s.*), deals with surgery of the lungs, thorax, heart, breast, spine, head, neck, face and mouth. There are also chapters on the urgent surgery of the blood vessels, control of hæmorrhage, compound fractures of the extremities, acute periosteomyelitis, joints, tendons and nerves, and a final chapter on gangrene. As in the preceding volumes, the illustrations are numerous and practical, and many are in colour.

The contents of the August issue, which will contain a symposium on 'Fertility and Infertility', will be found on page lxxii at the end of the advertisement section.

Notes and Preparations, see page 105.
Fifty Years Ago, see page 109

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NOTES AND PREPARATIONS

NEW PREPARATIONS

'ALLEVIN' is a compound preparation of salicylamide, caffeine and codeine, each tablet containing salicylamide, 7.5 grains (0.5 g.); caffeine, 1 grain (0.06 g.); and codeine, 0.119 grain (0.0007 g.). It is claimed that salicylamide possesses marked anti-rheumatic, analgesic and antipyretic properties, and does not irritate the gastric mucosa. Indications for the use of 'allevin' include painful rheumatic conditions, headache, neuralgia, dysmenorrhœa and menstrual pain, influenza and colds, sinusitis, and in dental surgery. (Herts Pharmaceuticals Ltd., Welwyn Garden City, Herts.)

AMENORONE' (ethisterone, 10 mg., and ethinylœstradiol, 0.01 mg., per tablet) has been prepared for the treatment by oral administration of primary and secondary amenorrhœa, menorrhagia and metrorrhagia, infertility, and habitual and repeated abortion. It is issued in boxes of 20 and bottles of 100 and 500 tablets. (Roussel Laboratories Ltd., 847 Harrow Road, London, N.W.10.)

'BEPHEN' tablets each contain phenobarbitone, 16 mg., and aneurine hydrochloride, 5 mg. They have been prepared for use in routine sedative therapy combined with correction of vitamin B deficiency in such conditions as neurasthenia, thyrotoxicosis, gastro-intestinal disorders, peptic ulcer, hypertension, arteriosclerosis, and in the aged. (Menley & James Ltd., Coldharbour Lane, London, S.E.5.)

'HYDERGINE' consists of equal parts of the three alkaloids dihydroergocornine, dihydroergocristine, and dihydroergokryptine, but, unlike the natural alkaloids of ergotoxine, they produce vasodilatation instead of vasoconstriction. 'Hydergine' has been prepared for use in the treatment of hypertensive and peripheral vascular states, and is indicated in the treatment of hypertension, coronary insufficiency, toxæmia of pregnancy, phæchromocytoma, and peripheral vascular disease. Issued in two forms: as sublingual tablets, each containing 0.25 mg. of hydergine, and as a solution for parenteral injection, in ampoules of 1 ml. (0.3 mg. hydergine). (Sandoz Products Ltd., 134 Wigmore Street, London, W.1.)

'KATONIUM' is an ion exchange resin, a mixture of ammonium and potassium polystyrene sulphonates. It is claimed that when given by mouth 'it absorbs sodium ion in the gut and is active over a large segment of the gastro-intestinal tract'. Its use is thus indicated in conditions in which a low-sodium diet is required, such as congestive heart failure, hepatic cirrhosis, hypertension and nephrosis. Issued in the form of a powder, in tins of 1 lb. and 7 lb. (Bayer Products Ltd., Africa House, Kingsway, London, W.C.2.)

'PHENURONE' (phenylacetylurea) is a synthetic anticonvulsant for the treatment of epilepsy, and is stated to have proved particularly effective in the control of psychomotor seizures. Its use is also indicated in cases of *grand* and *petit mal*. In *grand mal* the incidence of improvement was found to be greater 'when the seizures occurred in patients who also experienced *petit mal* or psychomotor attacks'. 'Phenurone' must be used under strict medical supervision, as in some cases risks are entailed. (Abbott Laboratories Ltd., Perivale, Greenford, Middlesex.)

'PIPANOL' brand of benzhexol hydrochloride (1-phenyl-1-cyclohexyl-3-piperidyl-1-propanol hydrochloride) is a powerful spasmolytic which is stated to have a stimulating effect on the central nervous system and to be of low toxicity. The chief indication for the use of 'pipanol' is in Parkinsonism, particularly the post-encephalitic and arteriosclerotic types, in which marked control of rigidity, reduction in oculogyric crises, and a feeling of well-being are claimed. The drug is stated to be well tolerated. Issued in tablets of 2 mg. and 5 mg., in bottles of 100 and 250. (Bayer Products Ltd., Africa House, Kingsway, London, W.C.2.)

'PYCAZIDE', a preparation of isonicotinic acid hydrazide (pyridine-4-carboxylic acid hydrazide) for the treatment of tuberculosis, is issued in three forms: as tablets of 50 mg., in containers of 100, 500 and 1000; in ampoules of 2 ml., containing 50 mg. in sterile aqueous solution, in boxes of 12 and 50; and as a blackcurrant flavoured syrup, one teaspoonful of which is approximately equivalent to 20 mg. of isonicotinic acid hydrazide, in bottles of 20 and 80 fluid ounces. (Herts Pharmaceuticals Ltd., Welwyn Garden City, Herts.)

'STREPTOMYCIN SULPHATE' Glaxo is 'a highly refined preparation of the antibiotic *Streptomyces griseus*', and is stated to possess an exceptional degree of purity which 'ensures relative freedom from pain on injection and from histamine-like reactions . . .' Its use is indicated in certain forms of tuberculosis and in some non-tuberculous infections which are not amenable to treatment with penicillin.

CONTINUED ON PAGE 106

Issued in cartons of 10 vials, each containing the equivalent of 1 g. streptomycin base (1 mega unit), and also in vials of 5 g. (Glaxo Laboratories Ltd., Greenford, Middlesex.)

NEW APPARATUS

THE 'SANOID' ROCKING STRETCHER for resuscitation has been produced to enable Eve's method of resuscitation to be carried out with ease. Advantages claimed for the rocking stretcher method of artificial respiration are: (1) the patient does not incur fractured ribs; (2) resuscitation can be applied despite existing fractures; (3) warmth can be applied to the patient during the resuscitation; (4) little effort is required from the operator; (5) no skill is necessary to operate the stretcher, 'as respiration is inevitable'. The 'Sanoid' rocking stretcher consists of a standard stretcher, attached to a trestle, which can be folded for easy transport. (Cuxson Gerrard & Co., Ltd., Oldbury, Birmingham.)

TREACHER COLLINS PRIZE ESSAY

THE subject for the next award by the Ophthalmological Society of the United Kingdom for this Prize of £100 is 'The Eye in General Vascular Disease'. The prize is open to qualified medical practitioners of any nationality. Essays, to be written in English, should be submitted to the Hon. Secretary of the Society, 45 Lincoln's Inn Fields, London, W.C.2, by December 31, 1953.

HUNTERIAN SOCIETY GOLD MEDAL

THE subject for the 1952 essay is 'The Management of Hypertension in General Practice'. Further details are obtainable from the Hon. Secretary, Mr. Alec W. Badenoch, F.R.C.S., 110 Harley Street, London, W.1. The Society's Gold Medal for 1951 has been awarded to Dr. G. M. Temple Tate, of Mansfield, Notts., and a *proxime accessit* award has been made to Dr. M. Soloman, of Bootle, Liverpool.

CENTENARY OF THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET

THE Centenary of the Hospital for Sick Children, Great Ormond Street, was celebrated on Tuesday, May 27, when a thanksgiving service was held at St. Martins-in-the-Fields. H.R.H. The Princess Royal, Patron of the Hospital, after attending the thanksgiving service, proceeded to the Hospital where she unveiled a statue of St. Nicholas (by Mr. Gilbert Ledward, R.A.), in memory of the late Viscount Southwood, Chairman of the Hospital from 1939 to 1946, and then laid the foundation stone of the new Out-Patient Department.

PHOTOGRAPHY AND ART IN MEDICINE

AN exhibition of medical illustration—the first of its kind to be presented in this country by the Medical Group of the Royal Photographic Society of Great Britain and by the Medical Artists' Association of Great Britain—was held last month in London. Designed to show the contribution which the photographer and the artist can make to the service of medicine, this exhibition of over 300 items includes wax models, colour prints and transparencies, composite museum exhibits, and large teaching panels. It will be opened in the Histological Laboratory, Manchester University Medical School, by Sir Geoffrey Jefferson on July 5, and visitors will be admitted from July 7 to 19, from 10 a.m. to 6 p.m., 1 p.m. on Saturdays. The Chairman of the Medical Group of the Royal Photographic Society, which has some 250 members, is Sir Harold Gillies, and the President of the Medical Artists' Association is Sir Cecil Wakeley, Bt., P.R.C.S.

PUBLICATIONS

Emergency Bed Service.—The report for the year ended March 31, 1952, pays tribute to the Chairman, the late Dr. Geoffrey Evans, who has been succeeded by Dr. G. F. Abercrombie. The Service has now reached the peak in its daily work of admitting urgent cases to hospital. During the year reviewed, 47,653 general acute, 12,088 infectious, and 3,120 chronic sick cases applied for admission to the London offices. During the winter of 1950-1 the average time needed to admit a case was 34 minutes; in 1951-2 it was 29 minutes. (King Edward's Hospital Fund for London, 10 Old Jewry, London, E.C.2.)

Ida S. Scudder of Vellore, by Mary Pauline Jeffery, M.D., is the affectionately written biography of one who can best be described as the 'Grand Old Lady' of Vellore. As founder of the Christian Medical College of Vellore, 'Dr. Ida' can look back with pride upon the result of her fifty years in India. The daughter of an American medical missionary who devoted his life work to India, she entered upon a family tradition of Christian service, particularly to the women of India. The impressive buildings of the Medical College are a tribute to the zest, courage and determination with which she overcame all difficulties and inspired all who worked with her. (Friends of Vellore, Annandale, North End Road, London, N.W.11, price 6s.)

The Treatment of Acute Dehydration in Infants, by a Working Team appointed and advised by the Committee on Acute Infections in Infancy.

CONTINUED ON PAGE 108

THE CHEMOTHERAPY

TB

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Medical Research Council Memorandum, No. 26.—As infants lose fluids readily and as they are subject to many vomiting and diarrhœal conditions, it is not surprising that in recent years many lives have been saved by speedy treatment of dehydration by the giving of fluids and electrolytes intravenously, orally and intramuscularly. The memorandum deals with the clinical and chemical assessment of dehydration, and then gives clear and practical guidance for this treatment—all summarized in a separate chart within a folder. This is a most useful memorandum for all interested in infants and children. (H.M. Stationery Office, price 3s.)

The Threshold of the Abnormal: A Basic Survey of Psychopathology, by Werner Wolff.—The subtitle of this book is more descriptive than the title, and it is a laborious survey. There are eighteen chapters and at the end of each is a long list of references; 316 is the top score. It is really a reference book and a good guide to references. But it tries to be all things to all men, a cosy book for the practitioner and an intriguing one for the man in the street; the former will find it like wedding-cake, a little goes a long way, the latter will look up his own vices, be a bit puzzled, and then put the book permanently aside. Any book on psychopathology, a subject almost as wide as the human world itself, but now heavily theorized, necessitating a jargon, and still a long way from its grand simplification, the exposition of its natural history, is most unlikely to make a universal appeal. Besides, this book ignores one small but important psychological point—Jones who never gives his own opinion, but is for ever quoting Smith, Brown and Robinson is a bore. This book is pure Jones. (Medical Publications Ltd., price 30s.)

The Story of Plastic Surgery, by George Bankoff, M.D., F.R.C.S.—The author's style is racy enough to attract: the historical introduction shows the whole course of surgery leading to a triumphant climax in the marvels of the modern plastic surgeon, and the second half describes and illustrates these feats with sufficient detail to tempt the sufferer from any real or fancied blemish to 'have a go'. The book, taken as a whole, leaves the impression of the notice on Mr. Wall's tricycles, 'Stop me and buy one'. (Faber & Faber, price 18s.)

Cancer.—Messrs. E. & S. Livingstone, Limited, have taken over the agency for Great Britain and the Commonwealth of *Cancer*, the bimonthly Journal of the American Cancer Society. The aim of this periodical is to give precedence to those papers concerned with human cancer or those which, although dealing in the experimental field, possess some suggestion bearing on human disease or the cancer problem as a whole. Each issue contains selected cancer abstracts. Subscription price £4 10s. annually, post free.

Copies of the new illustrated catalogue of books published by E. & S. Livingstone Ltd. will be sent to any one interested. (16-17 Teviot Place, Edinburgh.)

Colloquium on the Chemotherapy of Tuberculosis.—In July 1951 the Medical Research Council of Ireland held a colloquium in Dublin on the chemotherapy of tuberculosis, a full report of which has now been published. The contents include: 'An organic chemist's approach to the chemotherapy of tuberculosis', by V. C. Barry; 'Experimental evaluation of antibacterial agents in tuberculosis therapy', by W. H. Feldman; 'The chemotherapy of tuberculosis with thiosemicarbazones', by G. Domagk; 'The clinical evaluation of potential chemotherapeutic agents in pulmonary tuberculosis', by Marc Daniels. (Laboratories of Medical Research Council of Ireland, Trinity College, Dublin.)

Memoranda submitted to the Royal Commission on Marriage and Divorce by the National Marriage Guidance Council propose the provision of a definite medical service for premarital examinations as the *voluntary* privilege of those contemplating marriage. It is recommended that the minimum age of marriage should be gradually raised to at least seventeen. (78 Duke Street, Grosvenor Square, London, W.1, price 2s.)

Hot Water for Health.—The Gas Council's illustrated booklet, 'Hot Water for Health', gives a number of useful hints on the benefits derived from the use of hot water in the home, and information on economical methods of obtaining hot water on tap with the help of gas. (Obtainable free from local gas showrooms and from the Gas Council, 1 Grosvenor Place, London, S.W.1.)

The Medical Directory 1953.—The Editor of the *Medical Directory* writes:—

'The accuracy of the Medical Directory depends on the return of the annual schedule, which has recently been posted to members of the medical profession. Should the schedule have been mislaid I will gladly forward a duplicate on request. The full name of the doctor should be sent for identification. Communications should be addressed to the Editor, the Medical Directory, 104 Gloucester Place, London, W.1'.

THE PRACTITIONER: Fifty Years Ago, see page 109

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Half their remedies cured you dead—
Most of their teaching was quite untrue'.—
Rudyard Kipling: *Rewards and Fairies.*

JULY, 1902

To those looking forward—scientifically as well as gastronomically—to attending the joint meeting of the British Medical Association and the Irish Medical Association in Dublin this month, the editorial comments on the Manchester meeting of the B.M.A. fifty years ago, will be of particular interest:—'Manchester is famous for "monster meetings", and it appears to be the aim of those in whose hands the arrangements are to make the coming gathering of the medical clans worthy of that description . . . it seemed at one time as though the meeting would have to be abandoned lest it should break up in most admired disorder. Thanks mainly to the tact and conciliatory spirit of the president-elect, Mr. Walter Whitehead (of Whitehead's operation fame), the difficulties have to some extent been smoothed over for the present. It is understood that the "brass band" will cease for a time to cleave the general ear with its braying, and—for a strictly limited period—the wolf has consented to lie down with the lamb. It is not, however, a state of peace, but merely a partial suspension of hostilities, and in October the dogs of war are again to be let loose. In the meantime they are snarling at each other and tugging at their chains'. Apparently, as a final shot before the truce, the Lancashire and Cheshire Branch of the B.M.A., 'which marches to the music of the "band" ', had issued 'what is called a "reply" to the powerful indictment by Professor Japp Sinclair and his colleagues at the Southern Maternity Hospital against the Council of the Association, which allowed itself to be misled into hurling a feeble and ineffective thunderbolt that came back on its own head'. The Editor goes on to express his sympathy with Mr. Whitehead 'in the difficult position created for him by those who should have supported him in his efforts to make the annual meeting a success. But he may rest assured that the bulk of the Association do not wish their annual picnic to be disturbed by local squabbles'.

Commenting on the death of Dr. Levi Cooper Lane, Professor of Surgery in the Cooper Medical College, San Francisco, Malcolm Morris, who delivered the Lane Lectures the previous year, recalls that, when Lane presented himself as a candidate for the medical service of the U.S. Navy, 'his impromptu thesis was, to the surprise and consternation of his examiners, written in Latin'.

The first of the 'Original Communications', entitled 'The Causation of Carcinoma and Sarcoma', is by Alexander G. R. Foulerton, F.R.C.S., Lecturer on Public Health and Bacteriology at the Middlesex Hospital, and Director of the Cancer Research Laboratories.

Walter Whitehead, F.R.C.S.Ed. (1840-1913)

In this 'exhaustive paper', according to 'The Month', no reference is made to 'the most recent theory of the origin of cancer', which 'has been given to the world mainly through the medium of the public Press'. In a lecture delivered on June 11, Mr. Jonathan Hutchinson had referred to the increase of arsenic in medical prescriptions: 'Used mildly arsenic might be beneficial, but an undue use caused cancer in some cases, and in others greatly aggravated it'. He strongly condemned 'wall papers of a green colour, because there arsenic was prevalent, and cancer might ensue'.

FIFTY YEARS AGO—*continued*

The hero of 'Pioneers of Public Health' this month is Thomas Southwood Smith, 'to whose self-sacrificing labours we are largely indebted for the Public Health Act of 1848, which was almost the first serious attempt at legislation for the protection of the public against preventable disease'.

In Dr. Thomas J. Horder's review of diabetes mellitus the following passage is especially significant: 'With regard to the nature of the pancreatic lesion, the evidence for considering a *hyaline degeneration of the islands of Langerhans* as being the causal element in the production of the glycosuria, and, therefore, that it is this part of the gland which supplies the hypothetical glycolytic ferment, continues to grow'. Dr. Raymond Crawfurd, reviewing 'Diseases of the Circulatory System and Allied Disorders', abstracts a preliminary note on the possibility of treating mitral stenosis by surgical methods, by Thomas Lauder Brunton (*Lancet*, February 8, 1902), who had performed the proposed operation on the cadaver, and on the living heart of healthy cats. He was not privileged, however, to see his suggestion triumph over prejudice and ridicule. The credit of having translated Lauder Brunton's dream into reality belongs to the late Elliott C. Cutler of the Western Reserve University, Cleveland, Ohio.

Among the books on hygiene and public health, reviewed in *The Practitioner* fifty years ago, 'Hygiene and Public Health', by Louis Parkes and Henry Kenwood 'comes with good credentials, as the work of two writers who have long been identified with the successful teaching of Public Health students . . . That it is not a mere examination "cram-book" is sufficiently guaranteed by the names of the authors; and the teaching throughout is of the soundest, well brought up to date, and, considering the size of the book, wonderfully comprehensive and complete'. 'As compared with the Transactions of the various learned and medical societies, Hospital reports are like family records in their greater personal interest'. The 'most exhaustive communications' included in vol. 37 of *St. Bartholomew's Hospital Reports*, is 'that of Dr. Langdon Brown on Thrombosis and Inflammation of the Portal Vein; this essay gained the Raymond Horton-Smith prize as the best thesis presented for the degree of M.D. at Cambridge . . . and will serve as a most useful source of reference on the subject'.

Included in 'Practical Notes' are hints to officers selected for service in South Nigeria, drawn up by the Medical Adviser to the Government, according to whom 'Old Scotch or Irish whisky in great moderation, well diluted, and never taken on an empty stomach, is perhaps the least deleterious of spirituous liquors'.

W.R.B.

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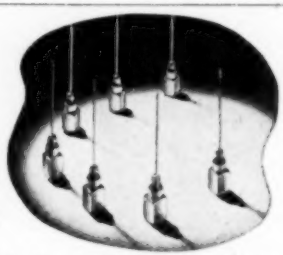

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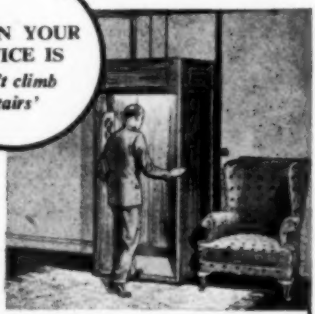

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By John C. T. Sanctuary, M.D., D.Obst.R.C.O.G.
Clinical Assistant, Obstetric and Gynæcological Department, King Edward VII Hospital, Windsor.

THE MALE FACTOR IN THE INFERTILE MARRIAGE
By H. A. Davidson, M.R.C.S., L.R.C.P.
Seminologist, Family Planning Association; Medical Officer in charge, Male Clinic, Philip Hill Parenthood Centre, Royal Northern Hospital; Seminologist, Whittington Hospital.

THE CERVICAL FACTOR IN FERTILITY
By H. H. Fouracre Barns, F.R.C.S., M.R.C.O.G.
Gynæcological Surgeon, Hospital for Women, Soho Square.

THE TUBAL FACTOR IN FEMALE SUBFERTILITY
By Linton Snaith, M.D., M.S., F.R.C.S., F.R.C.O.G.
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